Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

October 6th, 2021

(data current to October 2nd – 5th)

Biocomplexity Institute Technical report: TR 2021-107

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biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
  - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
  - Pandemic response for Influenza, Ebola, Zika, and others

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Overview

- **Goal**: Understand impact of COVID-19 mitigations in Virginia
- **Approach:**
  - Calibrate explanatory mechanistic model to observed cases
  - Project based on scenarios for next 4 months
  - Consider a range of possible mitigation effects in "what-if" scenarios
- **Outcomes:**
  - Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
  - Geographic spread over time, case counts, healthcare burdens

Key Takeaways

Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

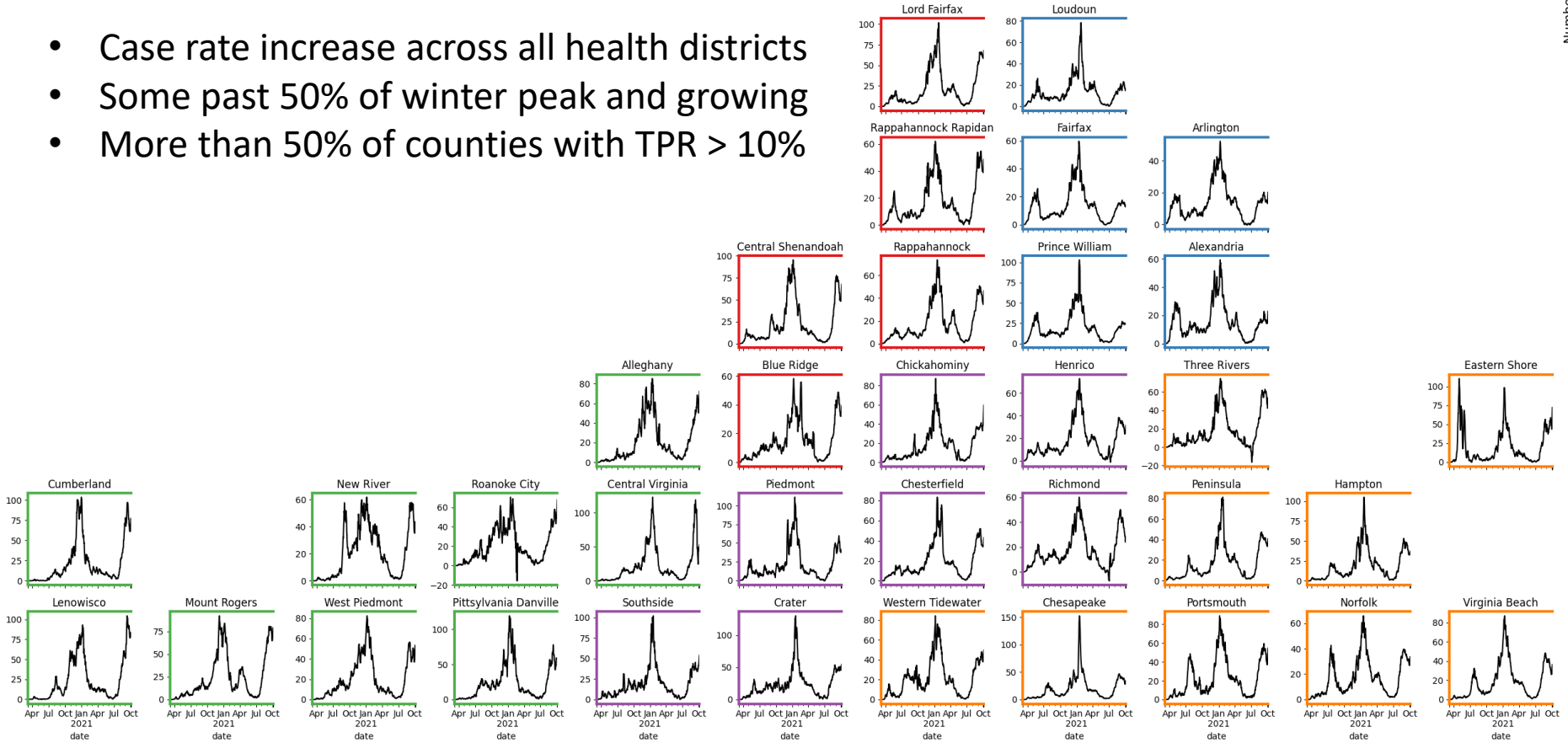
- **Case rates in Virginia continue to decline, with nearly all districts declining as well; case rates remain high and the rate of decline remains modest**
- VA 7-day mean daily incidence is slightly down to 32/100K from 35/100K; US is also slightly down to 39/100K (from 43/100K)
- Projections show continued decline, with a few districts showing some growth under current conditions
- Significant future case growth remains possible when tested with transmission drivers from last year
- Recent updates:
  - Analysis to show potential impact of Influenza based on past seasons
  - Prelim analysis of impact of expanded immunity through 3rd doses
  - Adjustment to higher levels of assumed immunity waning (natural and vaccine)

The situation continues to change. Models continue to be updated regularly.

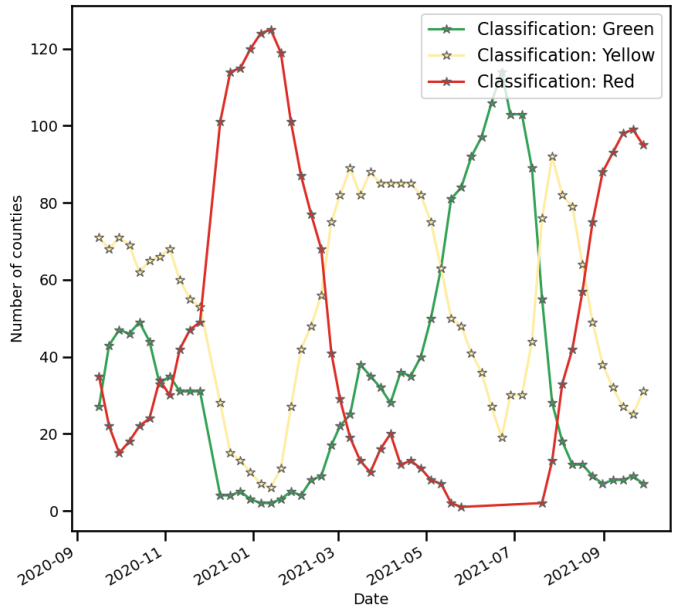
Situation Assessment

Case Rates (per 100k) and Test Positivity

- Case rate increase across all health districts
- Some past 50% of winter peak and growing
- More than 50% of counties with TPR > 10%



Data source: https://data.cms.gov/covid-19/covid-19-nursing-home-data



County level RT-PCR test positivity

Green: <5.0% (or <20 tests in past 14 days)

Yellow: 5.0%-10.0% (or <500 tests and <2000 tests/100k and >10% positivity over 14 days)

Red: >10.0% (and not "Green" or "Yellow")

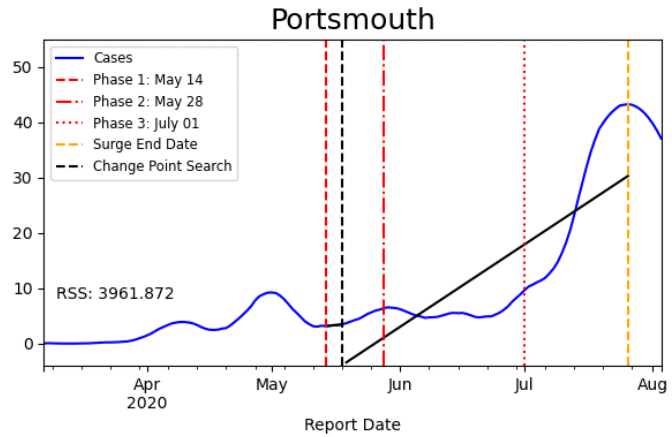
Classification	Green	Yellow	Red
date			
2021-06-28	103.0	30.0	0.0
2021-07-06	103.0	30.0	0.0
2021-07-13	89.0	44.0	0.0
2021-07-20	55.0	76.0	2.0
2021-07-27	28.0	92.0	13.0
2021-08-03	18.0	82.0	33.0
2021-08-10	12.0	79.0	42.0
2021-08-17	12.0	64.0	57.0
2021-08-24	9.0	49.0	75.0
2021-08-31	7.0	38.0	88.0

District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

Hockey stick fit

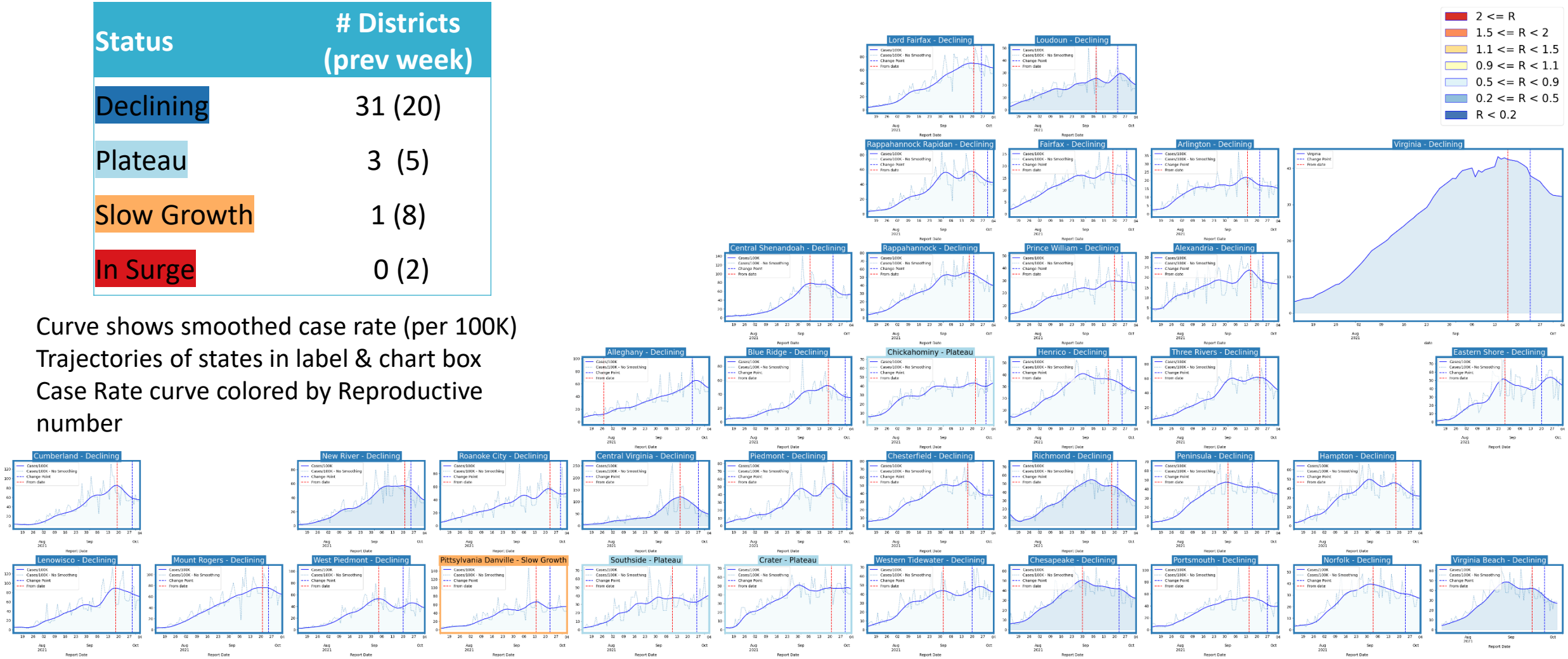


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	31 (20)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	3 (5)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	1 (8)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	0 (2)

District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	31 (20)
Plateau	3 (5)
Slow Growth	1 (8)
In Surge	0 (2)

Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive number



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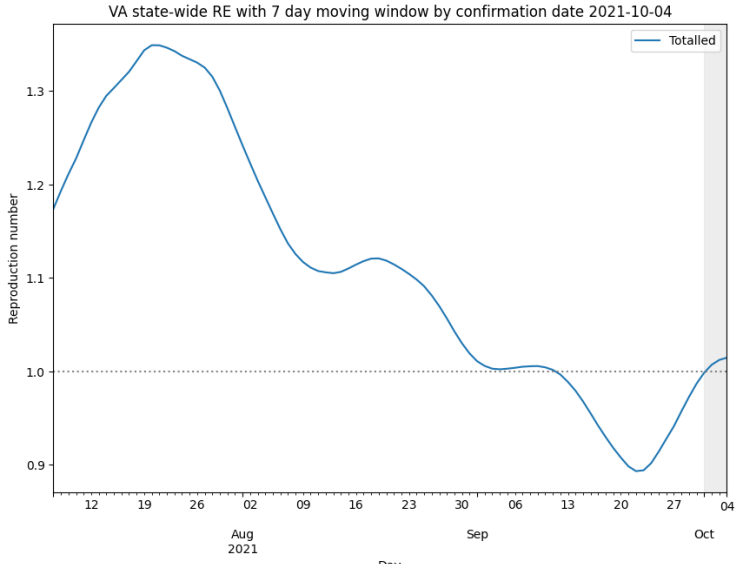
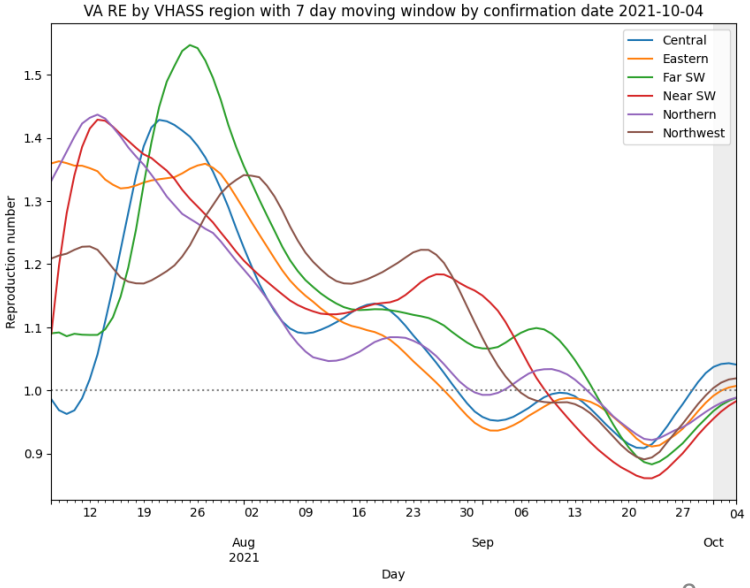
Estimating Daily Reproductive Number

October 4th Estimates

Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	1.015	0.037
Central	1.041	0.063
Eastern	1.007	0.013
Far SW	0.988	0.024
Near SW	0.983	0.042
Northern	0.989	-0.023
Northwest	1.019	0.069





Methodology

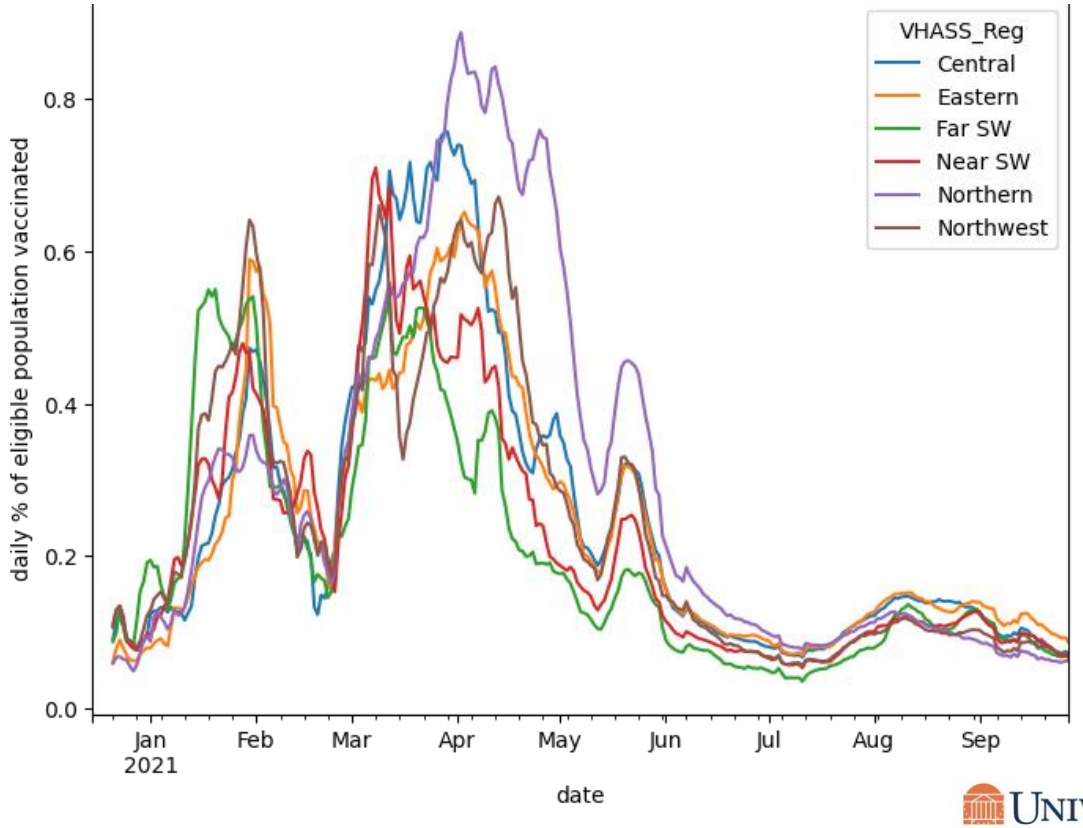
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

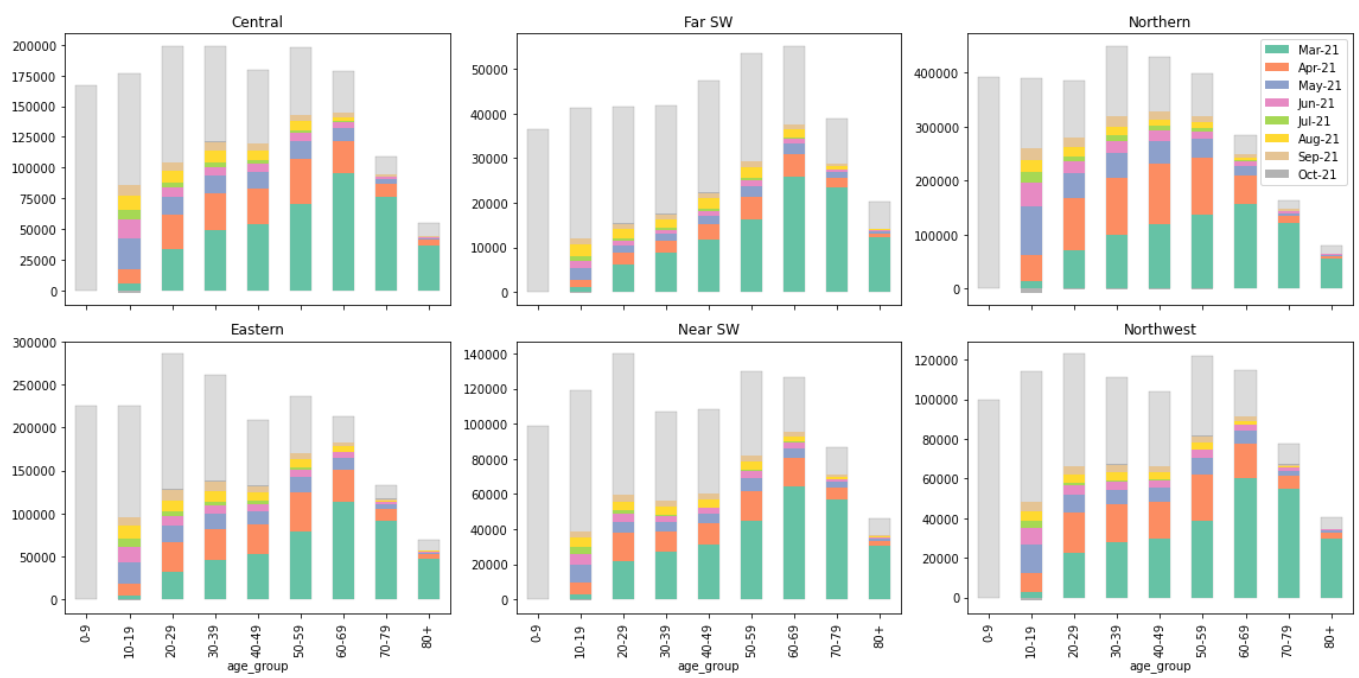
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Vaccination Administration Slow

Regional Vaccine courses initiated per day (% eligible):

- Proportion eligible for first dose of vaccines across regions (in the ~0.1% or 100 per 100K a day)
- Age-specific proportions of population vaccinated show recent progress in younger ages





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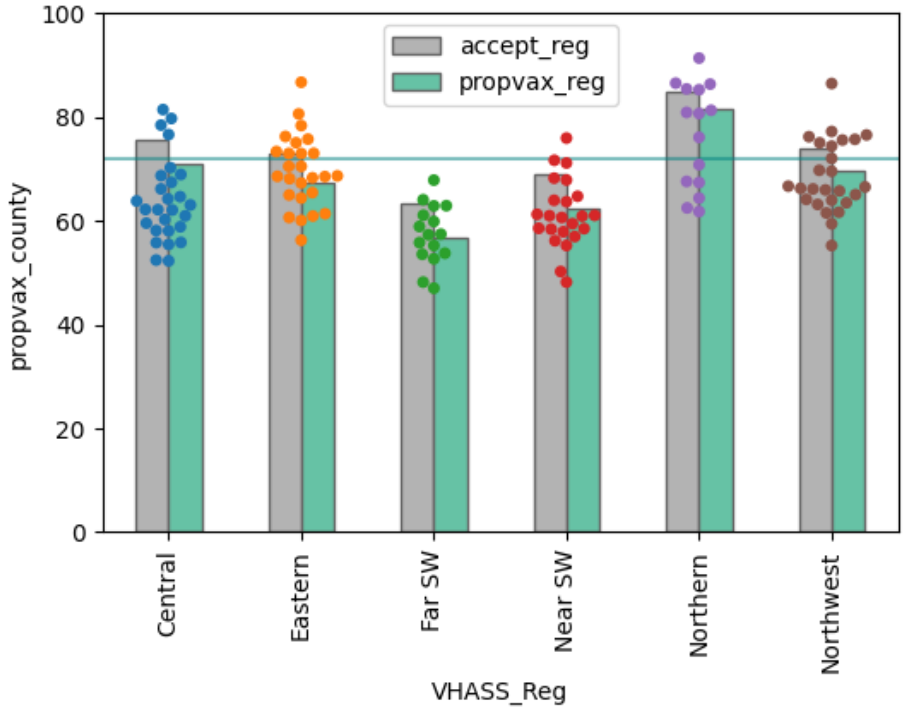
Vaccination Acceptance by Region

Corrections to surveys:

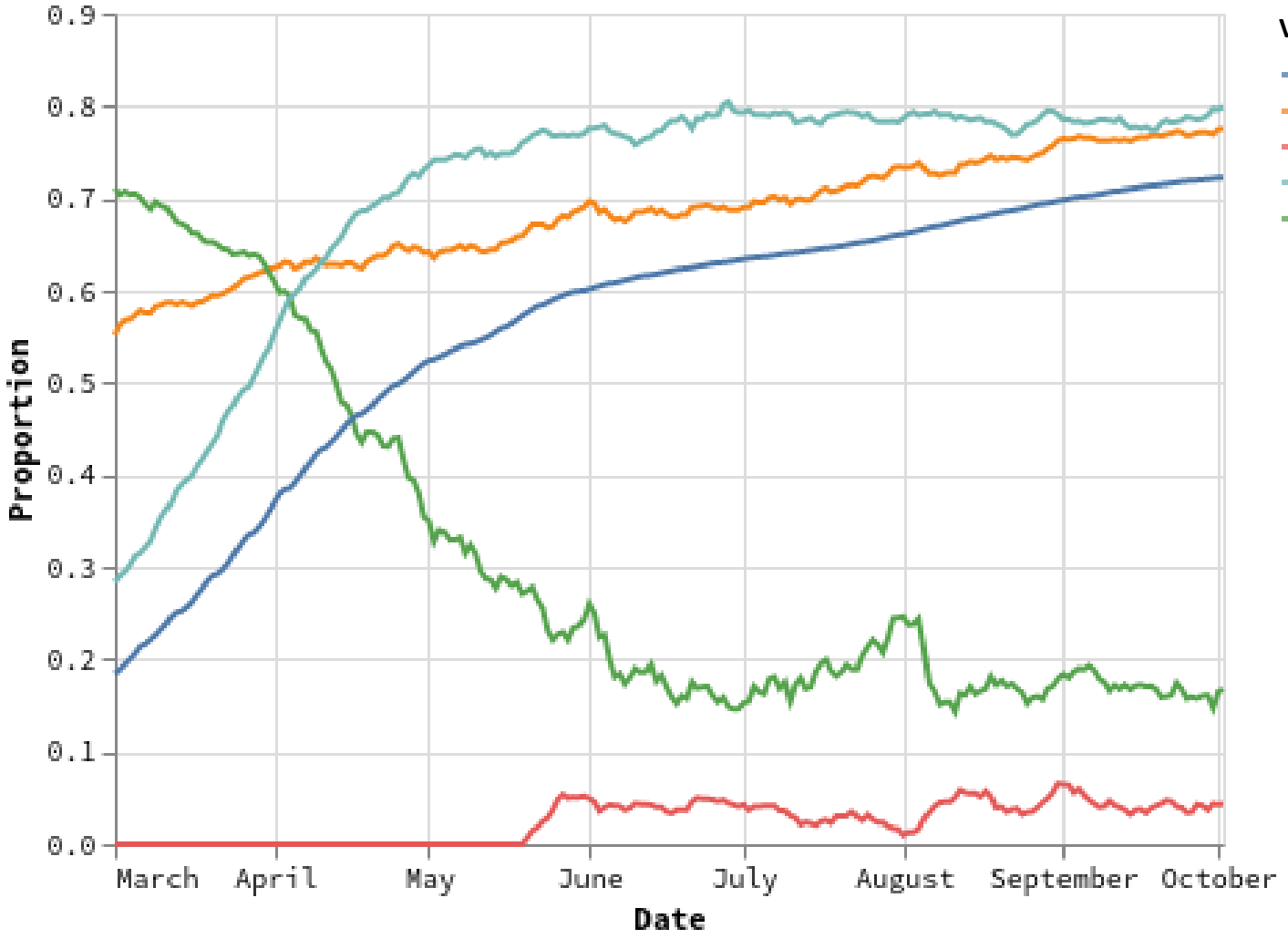
- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Correction approach:
  - Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
  - Cross-validate coarse corrections against HPS survey at the state level and corrected in same manner

Region	COVIDcast accepting corrected	VDH proportion pop vaccinated
Central	75%	71%
Eastern	73%	67%
Far SW	63%	57%
Near SW	68%	62%
Northern	86%	81%
Northwest	74%	69%
Virginia	**77%**	**72%**



Grey Bar: Survey measured and corrected acceptance
Green Bar: Proportion of eligible population administered a vaccine
Dots: Proportion administered at least one dose for each county

Vaccine Acceptance Components over Time



Vaccine Acceptance adjusted to include scheduled appointments

- Steady rise in acceptance over the past couple months
- Unvaccinated Acceptance shows ~20% of those who are unvaccinated are definitely or probably willing to be vaccinated
- Scheduled appointments for vaccination have increased through August but seem to be leveling off

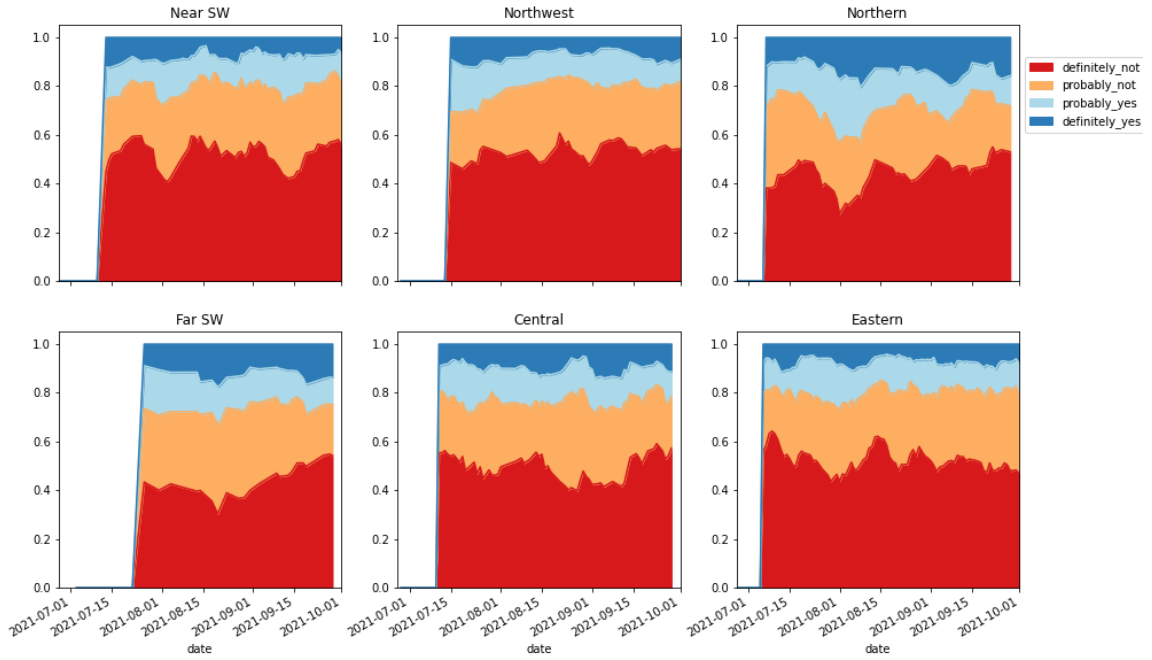
Data Source: https://covidcast.cmu.edu

Vaccine Acceptance by Region- COVIDcast

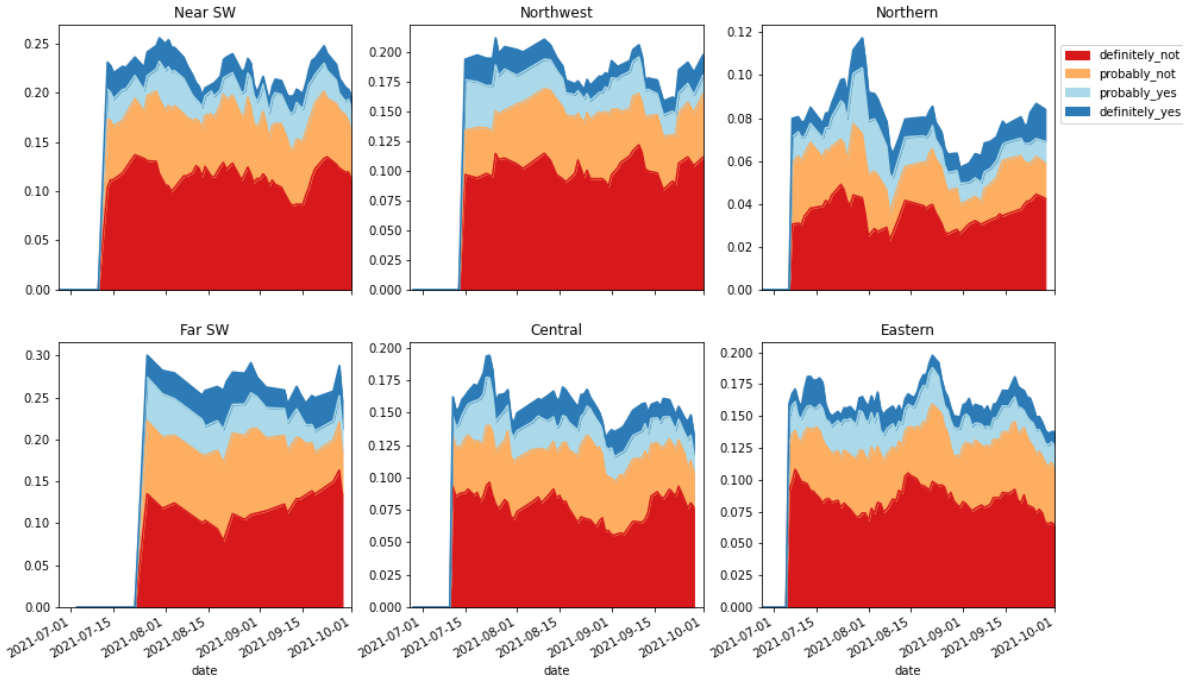
Levels of Acceptance and potential acceptance in flux:

- Most regions (except Central and Far SW) see vaccine uptake in the “Definitely Yes”.
- Among the unvaccinated, about 20-30% remain in the Definitely/Probably “Yes” categories.
- About 50% of the Unvaccinated seem to be in the “Definitely Not” category.

Unvaccinated Only



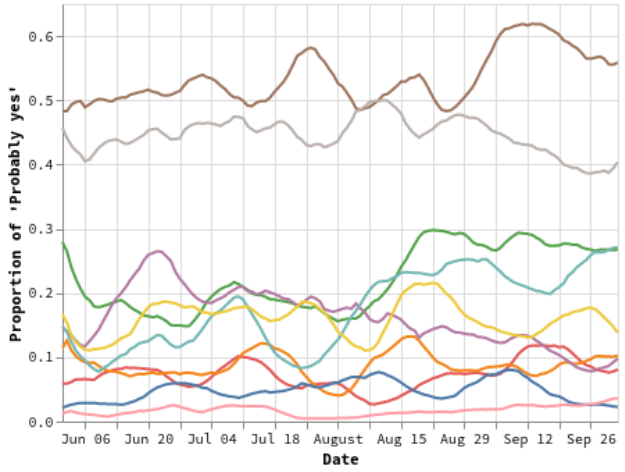
All Respondents



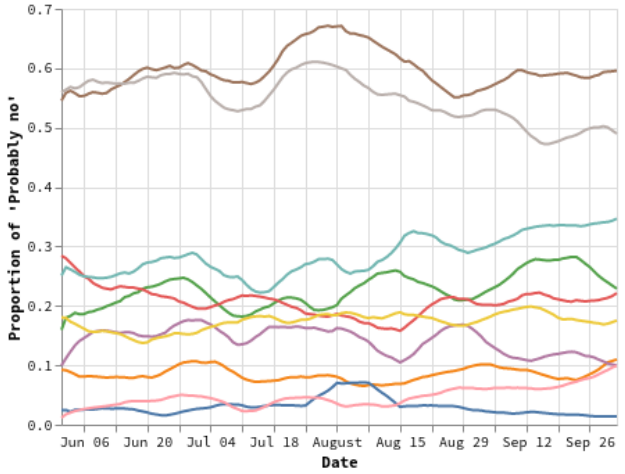
Data Source: https://covidcast.cmu.edu

Reasons for Hesitancy by Likeliness to Accept

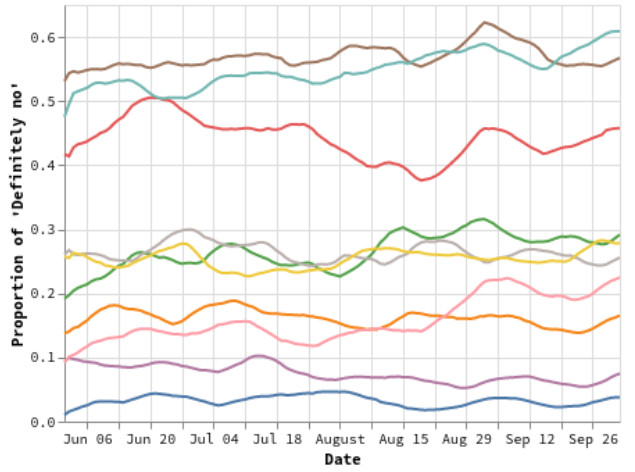
Probably Yes

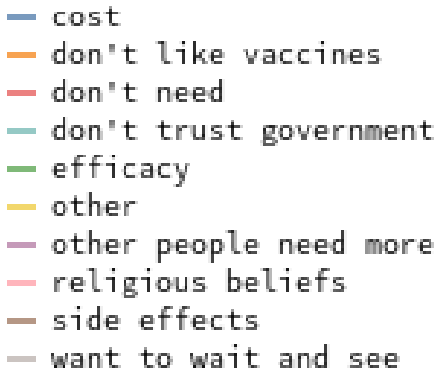


Probably No



Definitely No





Reasons for Hesitancy vary across tiers of likeliness to accept the vaccine

- Probably Yes and Probably No most concerned about side effects & are waiting to see
- Definitely No are concerned about side effects but also don't think they need the vaccine and don't trust the government, though don't need is declining
- Most other reasons are below 30% within these tiers of likeliness

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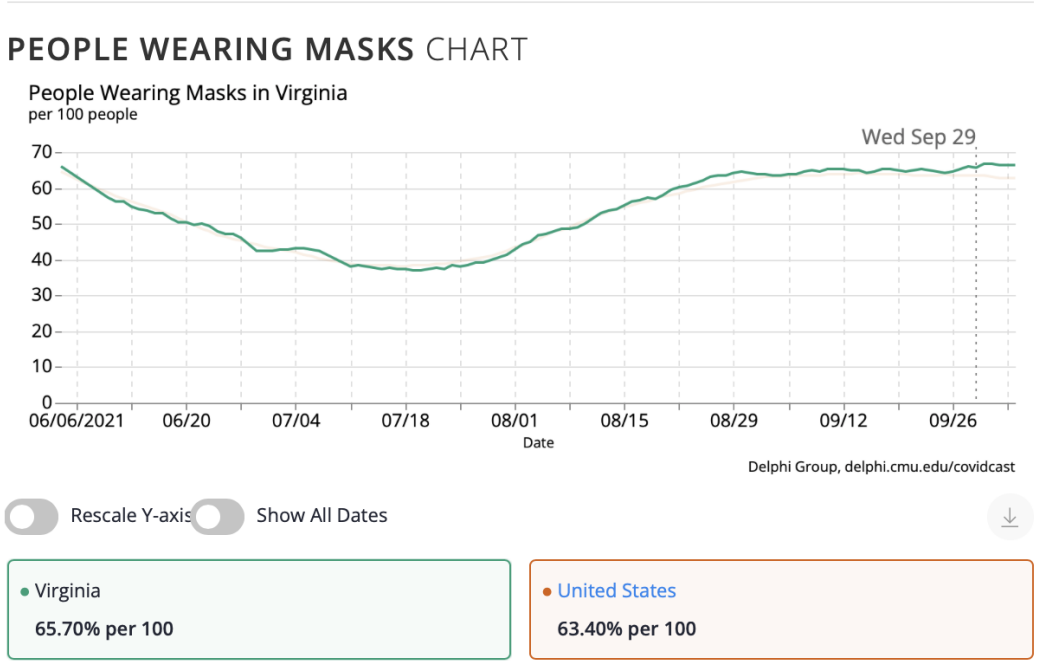
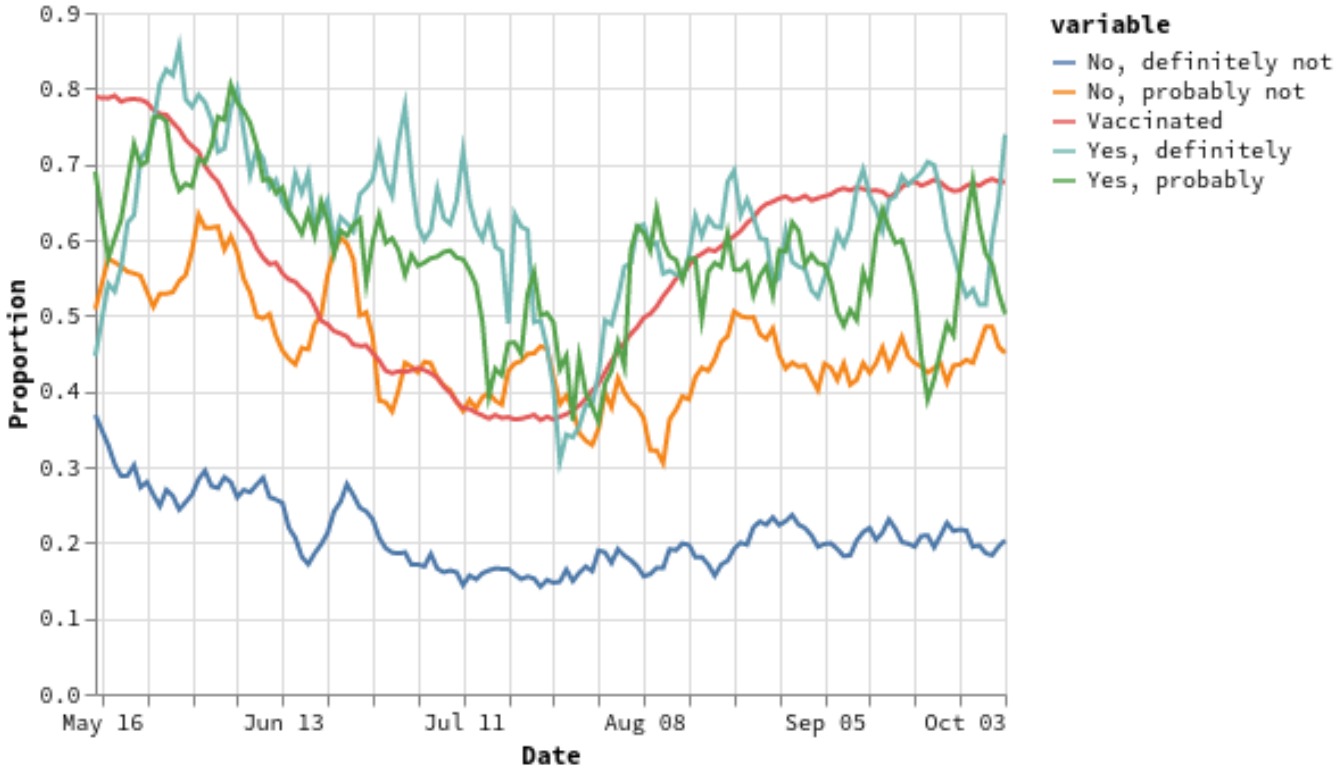
Data Source: https://covidcast.cmu.edu

Mask Usage Stalls

Self-reported mask usage has plateaued out to ~65%

- US and VA similar, though with considerable variation across counties and states
- Mask wearing remains lower amongst unvaccinated especially among least willing to be vaccinated





Data Source: https://covidcast.cmu.edu

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SARS-CoV2 Variants of Concern

Emerging new variants will alter the future trajectories of pandemic and have implications for future control

- Emerging variants can:
  - Increase transmissibility
  - Increase severity (more hospitalizations and/or deaths)
  - Limit immunity provided by prior infection and vaccinations
- Genomic surveillance remains very limited
  - Challenges ability to estimate impact in US to date and estimation of arrival and potential impact in future

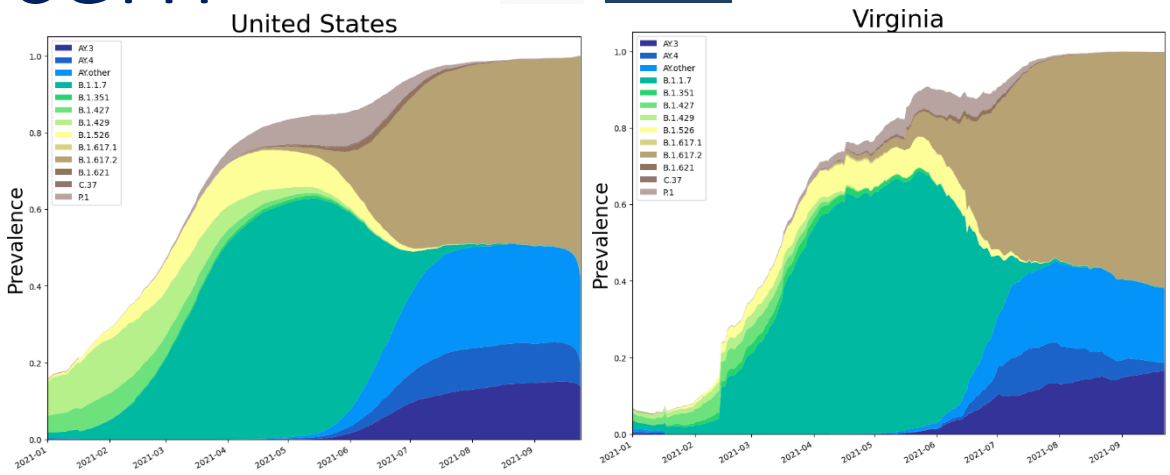
	New WHO Name	Transmissibility	Immune Evasiveness	Vaccine Effectiveness^
Ancestral		—	—	✓
D614G		+	—	✓
B.1.1.7	Alpha	+++	—	✓
B.1.351	Beta	+	++++	✓
P.1	Gamma	++	++	✓
B.1.429	Epsilon	+	+	✓
B.1.526	Iota	+	+	✓
B.1.617.2	Delta	++++*	++#	✓

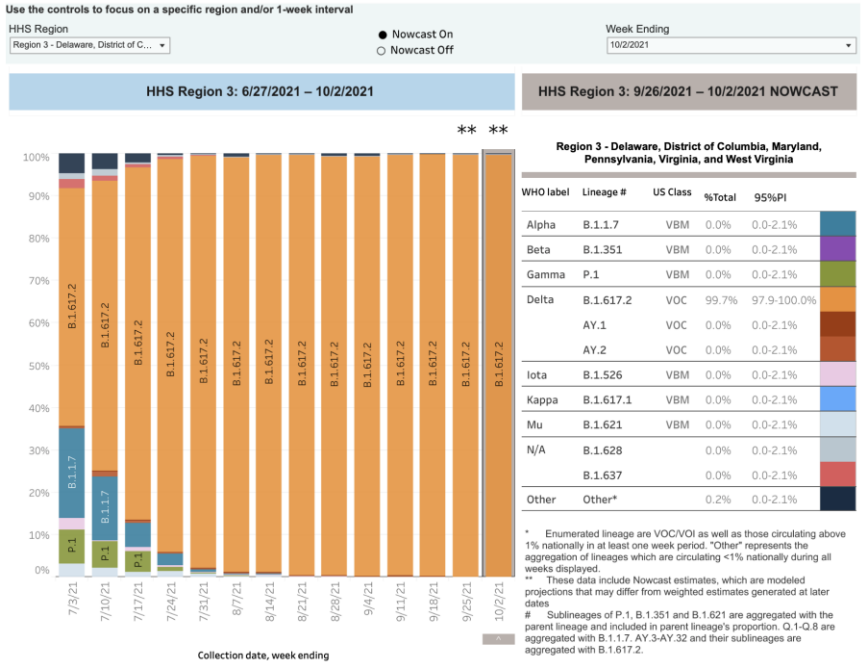
*Relative transmissibility to B.1.1.7 yet to be fully defined
^Effectiveness from real world evidence vs. severe illness, not all vaccines are effective vs all variants, and importance of 2-doses, especially for B.1.617.2 for which 1 dose of mRNA or AZ is only ~30% effective # May carry more immune escape than P.1, to be determined

World Health Organization

WHO and Eric Topol

GISAID outbreak.info



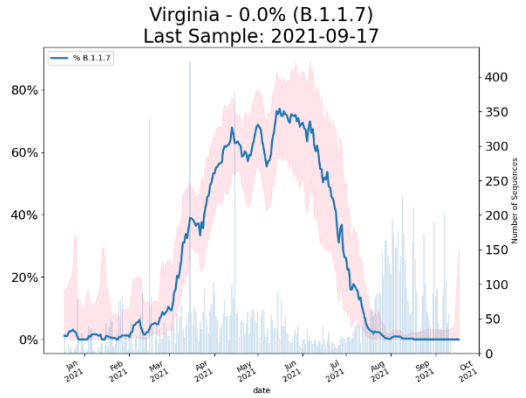


CDC Variant Tracking

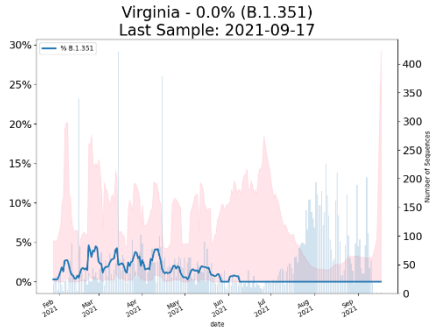
SARS-CoV2 Variants of Concern

Previous Variants

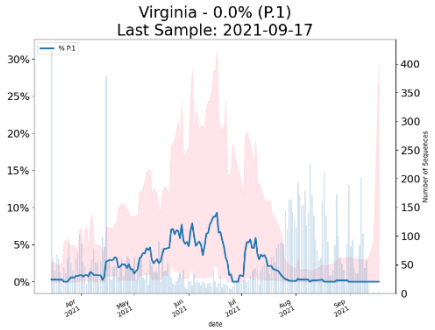
Alpha α - Lineage B.1.1.7



Beta β - Lineage B.1.351



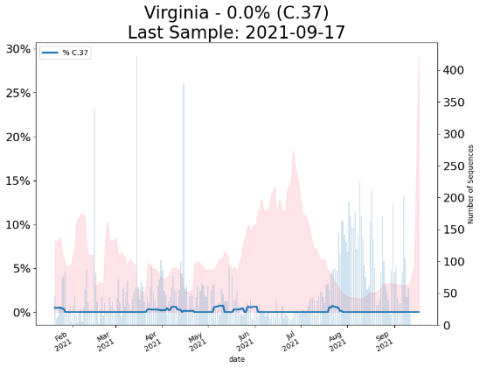
Gamma γ - Lineage P.1



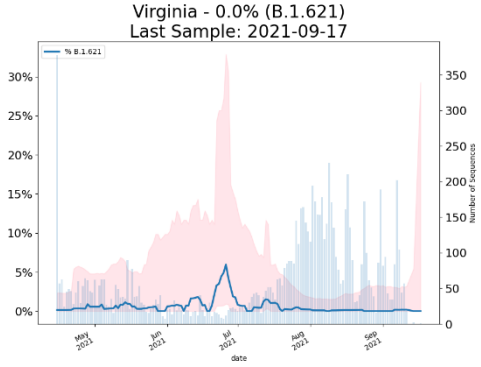
GISAID outbreak.info

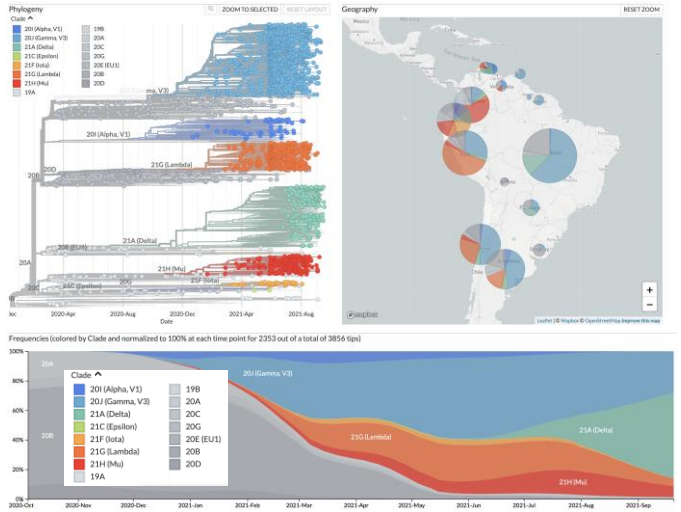
Emerging Variants

Lambda λ - Lineage C.37



Mu μ - Lineage B.1.621



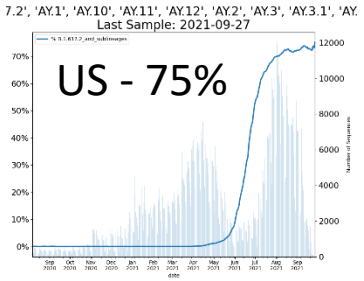


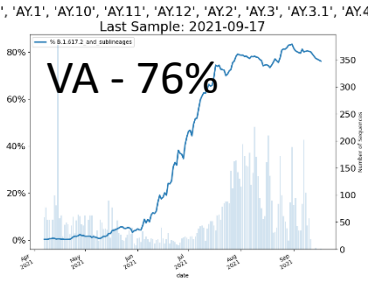
Delta continues to out compete Lambda and Mu in South America (over 50%, Lambda and Mu both below 10%)
Trevor Bedford Tweet & Nextstrain Analysis

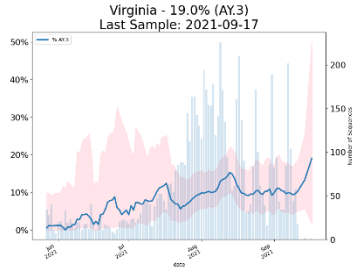
SARS-CoV2 Variants of Concern

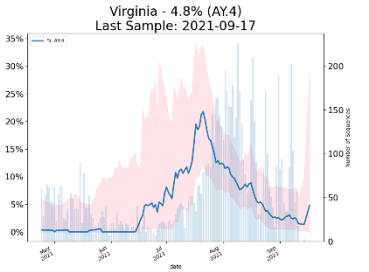
Delta δ - Lineage B.1.617.2 and related subvariants

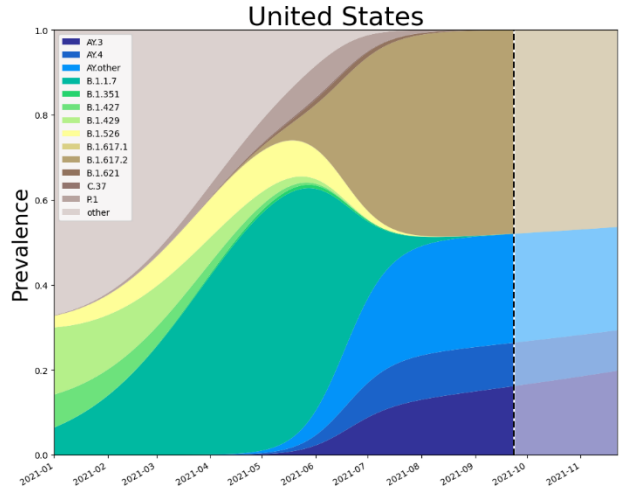
- Delta plus δ+ lineage which contains the K417N mutation is emerging as a sub-variant that is even more transmissible; declared a VoC in India
- Delta variant now dominates most of Europe and US
- CDC recommends resumption of mask wearing indoors due to reports of breakthrough infections of the vaccinated possibly being transmissible
- Recent study from Mayo clinic shows Delta reducing the efficacy of mRNA vaccines (Pfizer more so than Moderna) along with other reports. Israeli study showed 64% efficacy against infection, however, a 3rd dose may counteract this reduction
- Public Health Scotland study in Lancet suggests Delta is 2x more likely to cause hospitalization than Alpha
- Subvariants AY.3 grows slightly to the 15-20% range and AY.4 also slightly up to 2-5% range, these subvariants are mainly clustered in the US, others mainly outside of US









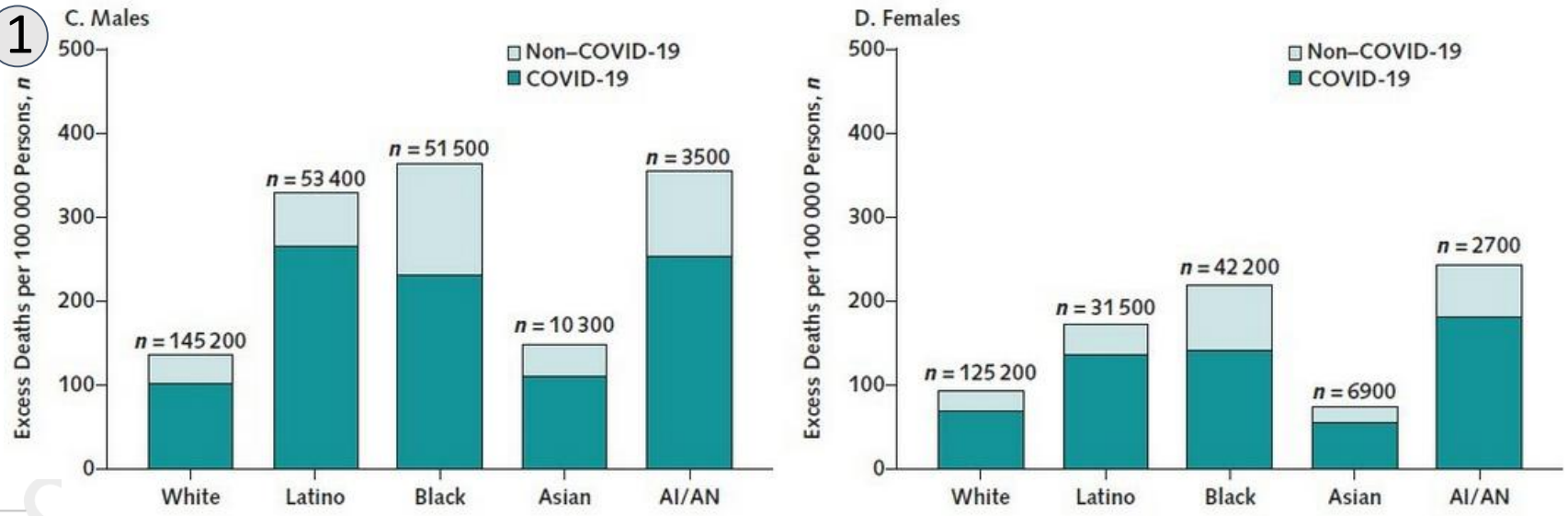


Current fits suggest stable mix of Delta & subvariants into the future

Variants & Vaccines

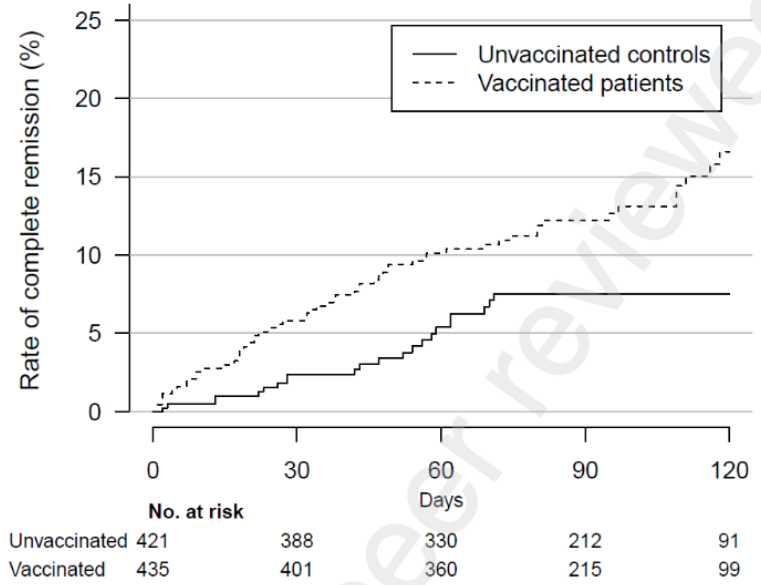
1. Profound racial/ethnic disparities in excess deaths in the United States in 2020 during the COVID-19 pandemic, resulting in rapid increases in racial/ethnic disparities in all-cause mortality between 2019 and 2020.
2. Reduction in vaccine effectiveness against SARS-CoV-2 infections over time is probably primarily due to waning immunity with time rather than the delta variant escaping vaccine protection.
3. COVID-19 vaccination lowers the severity and life impact of long COVID among patients with persistent symptoms.

1



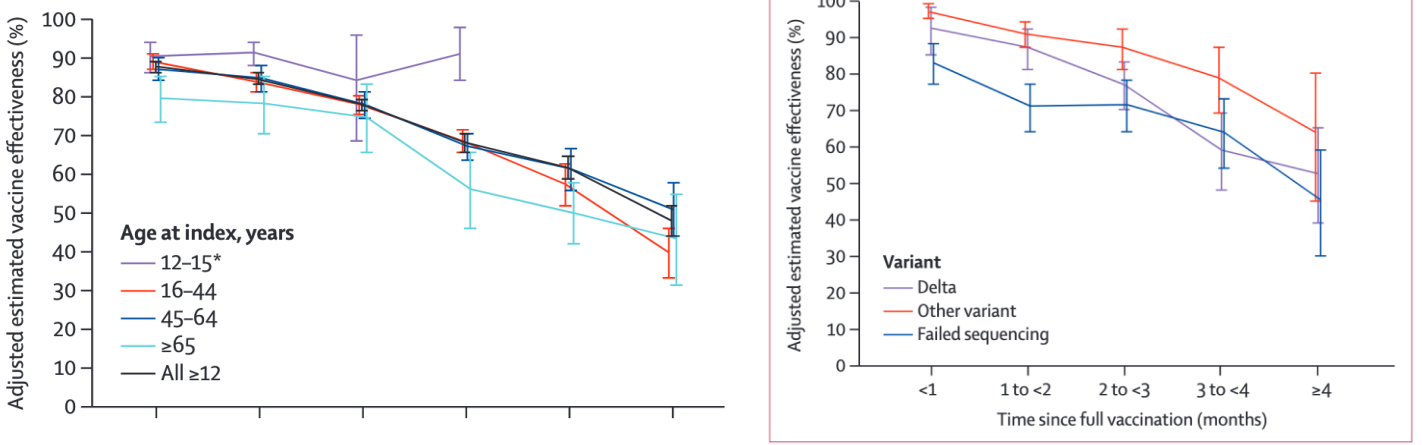
Scientists at the NIH recently analyzed mortality data from the CDC to characterize disparities around excess deaths due to COVID-19. Disparities in age-standardized deaths per 100 000 persons increased for Black and AI/AN males and females compared with White males and females
https://www.acpjournals.org/doi/10.7326/M21-2134

3



In this recent Lancet preprint French researchers emulate a target trial evaluating the effect of vaccination among patients with long COVID. 455 patients were allocated to the vaccination group and 455 to the control group; 545 (60·1%) had confirmed infections.
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3932953

2

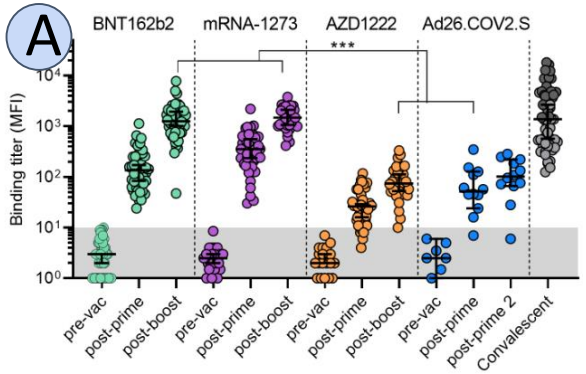


Pfizer funded study in Lancet study provides evidence for both robust effectiveness of Pfizer in children and waning immunity in older age groups regardless of variant.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02183-8/fulltext

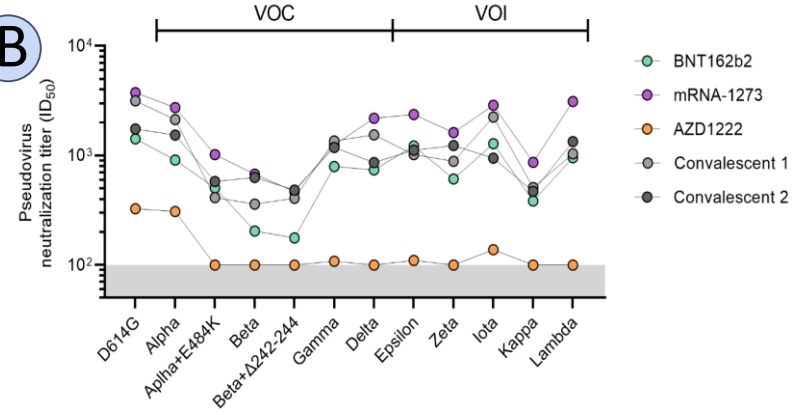
Variants & Vaccines

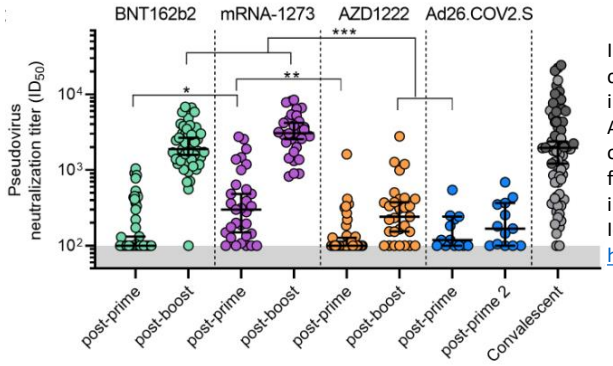
1. mRNA vaccines continue to show superior neutralization and binding profiles to that of adenovirus vector-based vaccines.
   a. **The proportion of individuals who did not show detectable VOC neutralization was substantial in the AZD1222 (AstraZeneca) and Ad26.COV2.S (J&J) recipients.**
   b. VOC neutralization was reduced in all vaccine groups,
2. Lancet study found second dose of mRNA after an Adenovirus (Pfizer with AZ) vaccine had higher efficacy than AZ alone (specifically AZ followed by Pfizer). Also saw higher immunogenicity of ChAd/BNT compared with ChAD/ChAd.
3. Science: Anti-viral defenses outside the human immune system shown to govern the severity of disease, illustrating a source of the highly variable severity of disease experienced. Based on a single SNP, OAS1 based defense is important to monitor for immune escape going forward (not based on spike protein sequence)

1 A



1 B

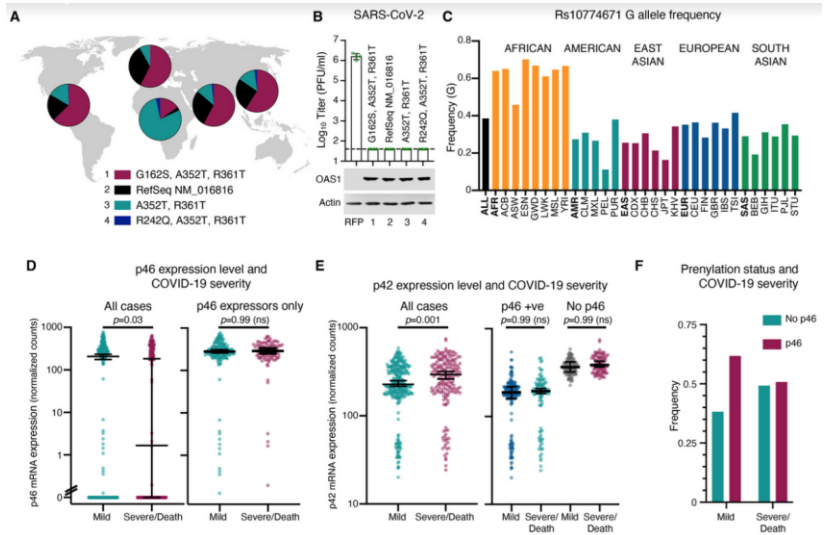




In a recent preprint researchers from Amsterdam showed results from a head-to-head comparison of the binding and neutralizing activity against all four VOCs in the serum of individuals who received the BNT162b2 (n=50), mRNA-1273 (n=40), AZD1222 (n=41) or Ad26.COV2.S vaccination (n=13). The largest (5.8-fold) reduction in neutralization being observed against the Beta variant. Introducing the E484K variant into Alpha resulted in a 2.8 fold reduced neutralization. This positional spike mutation seems to have a complementary impact only with certain other spike with configurations as observed in ID50 for Beta, Gamma, Iota, Zeta, Kappa (E484Q).
https://www.medrxiv.org/content/10.1101/2021.09.27.21264163v1.article-info

3

SNP (Rs10774671) governs whether people express either (A) prenylated OAS1 isoforms that are membrane-associated and sense specific regions of SARS-CoV-2 RNAs, or (B) only express cytosolic, nonprenylated OAS1 that does not efficiently detect SARS-CoV-2. (A) has been associated with protection from severe COVID-19.
https://www.science.org/doi/10.1126/science.abj3624



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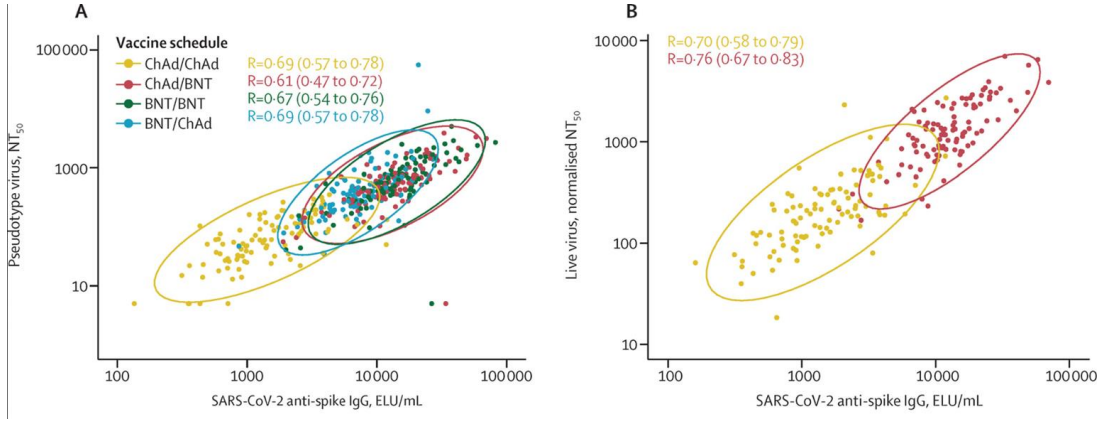
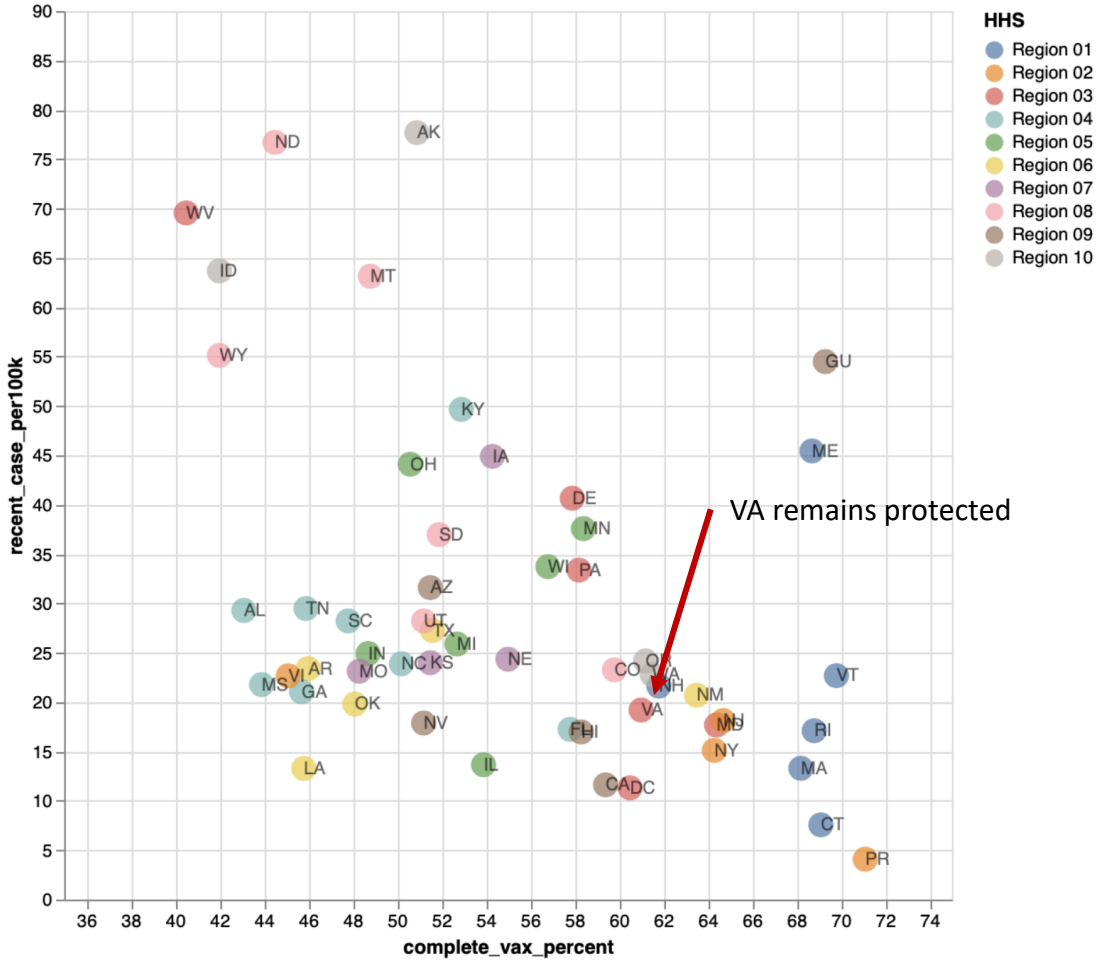


Lancet study provides evidence for benefit of heterologous vaccine schedule. Between Feb 11 and Feb 26, 2021, 830 participants were enrolled and randomised in a study by the Oxford vaccine group.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01694-9/fulltext#%20

Recent Cases Correlate with Vax Coverage

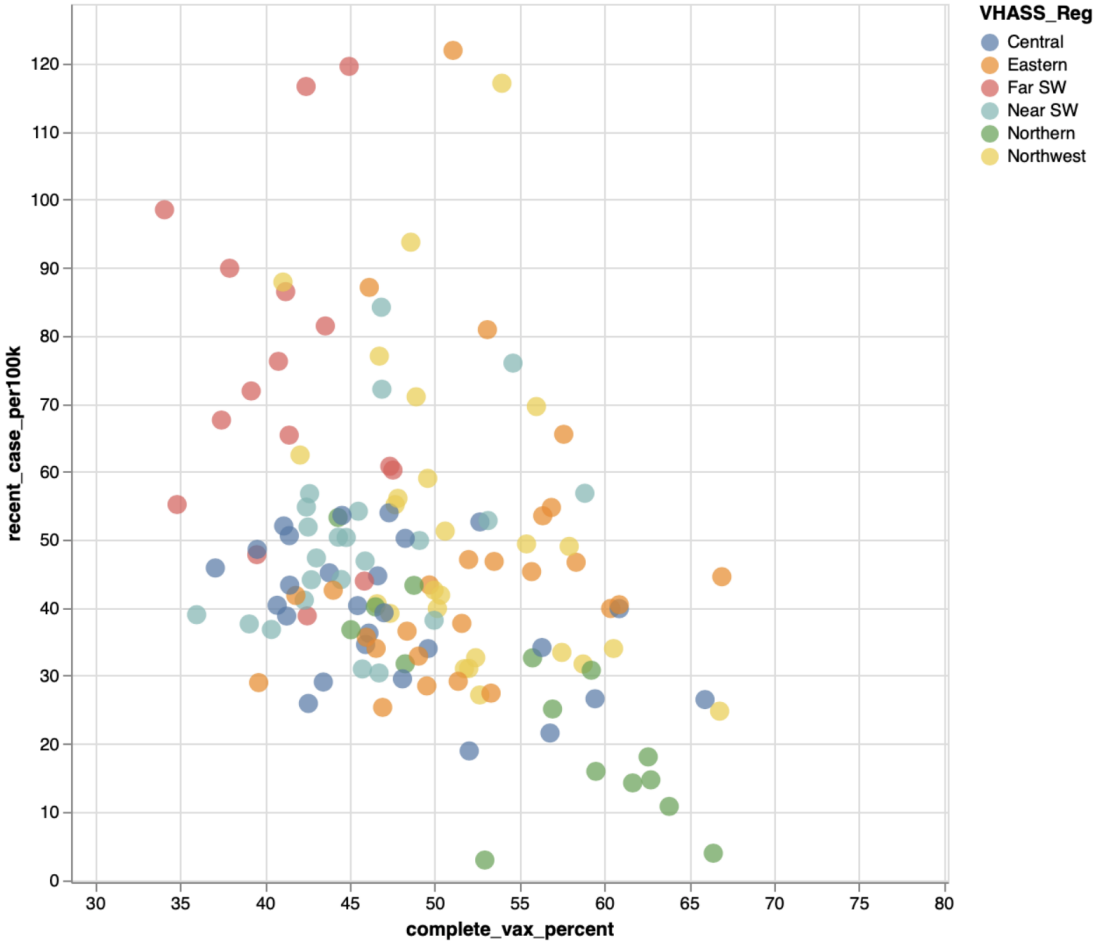
Mean cases per 100K vs. vaccine coverage

- States with lower vax coverage have had the worst case spikes



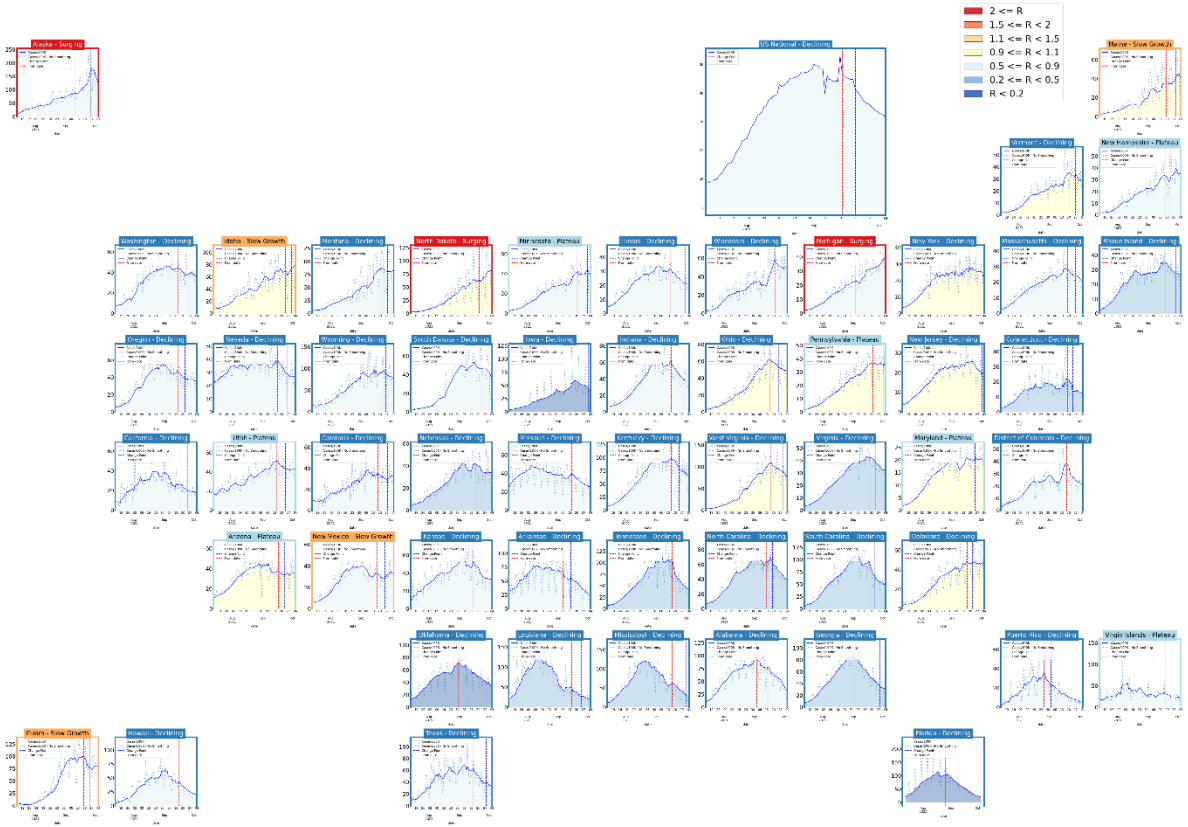
Virginia Counties

- Counties with higher vax coverage are maintaining lower case rates



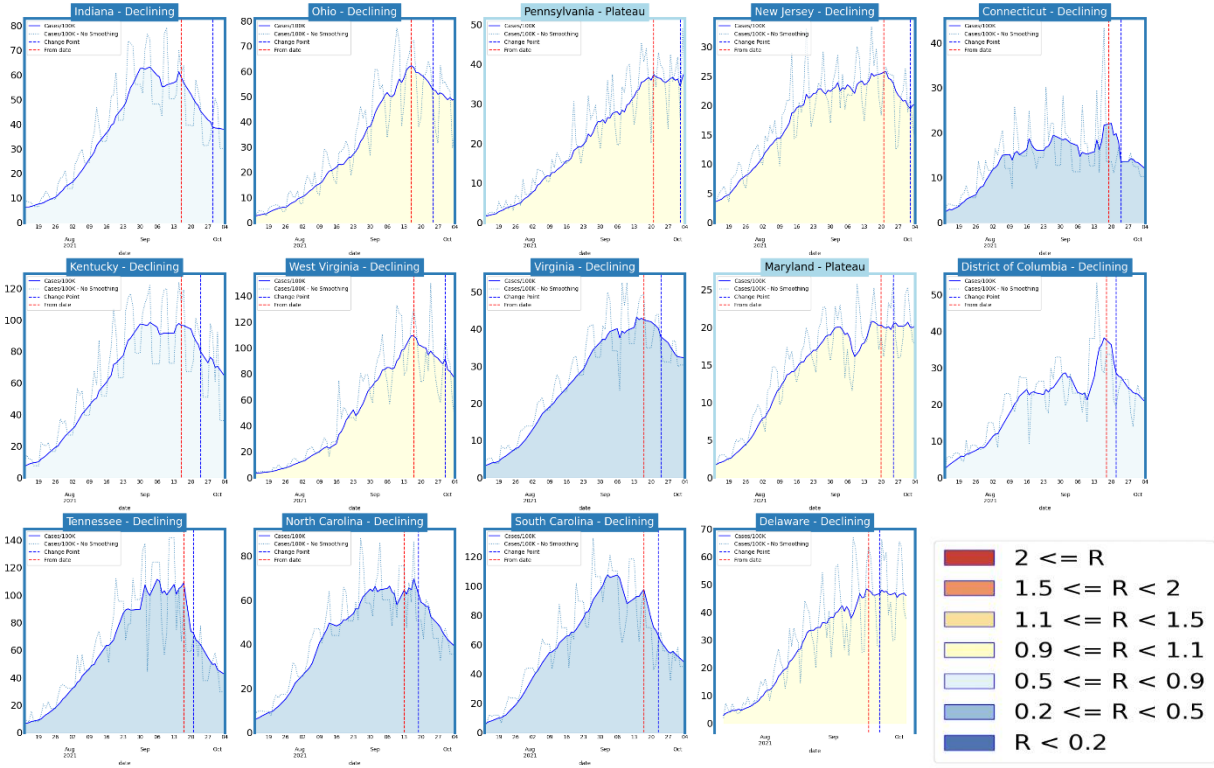
Other State Comparisons

Trajectories of States



- More of the country has plateaued and started to decline
- Some states remain in surge, but show signs of slowing
- Case rates remain very high, but nationally rates have had several weeks of sustained decline

Virginia and her neighbors

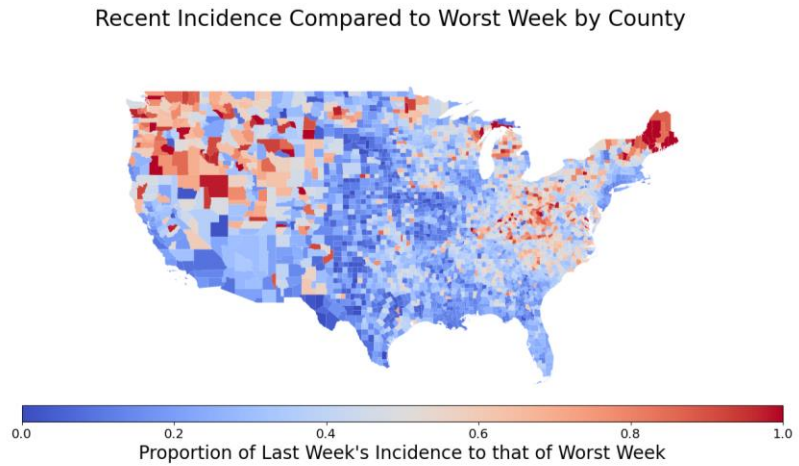


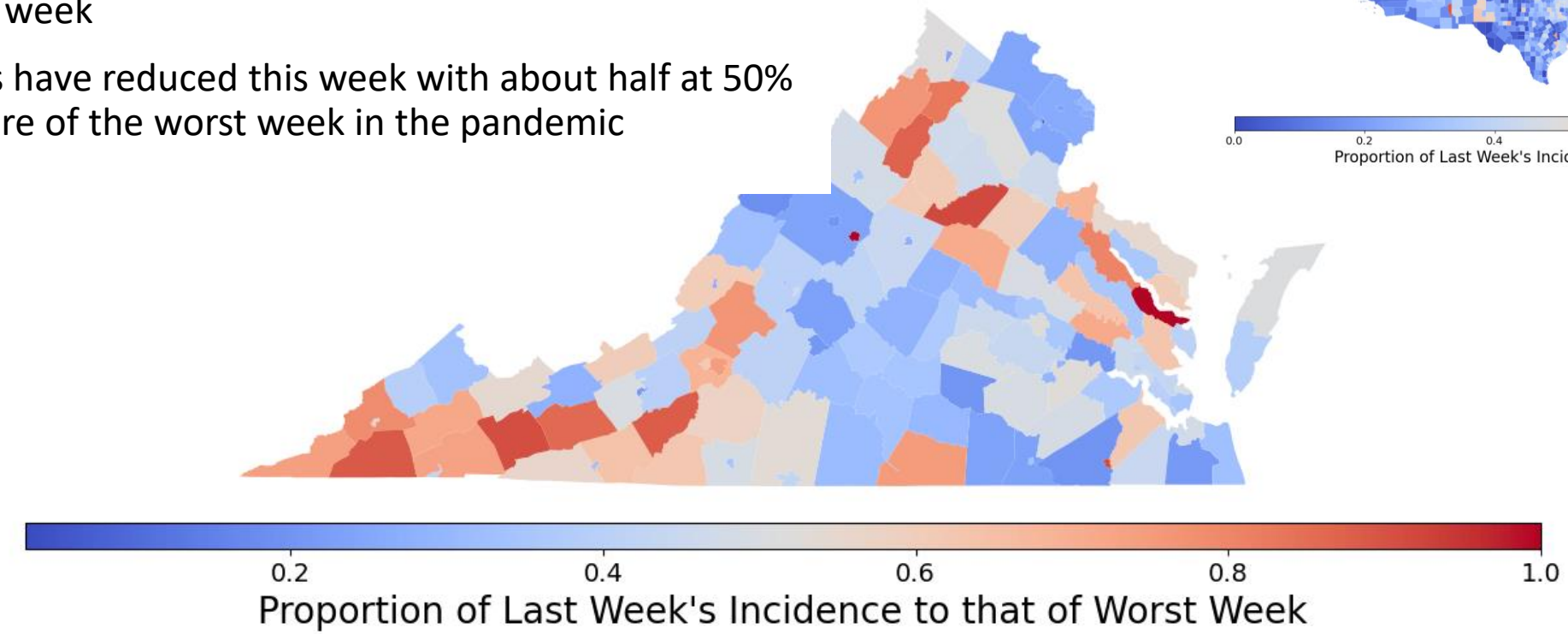
- Nearly all states now in sustained decline in the past week
- Case rates remain high

Last Week compared to worst week of Pandemic

County level Case Rates (per 100K) from this week compared to worst week of the entire pandemic

- Many counties exceed or have similar rates to the worst week
- Ratios have reduced this week with about half at 50% or more of the worst week in the pandemic





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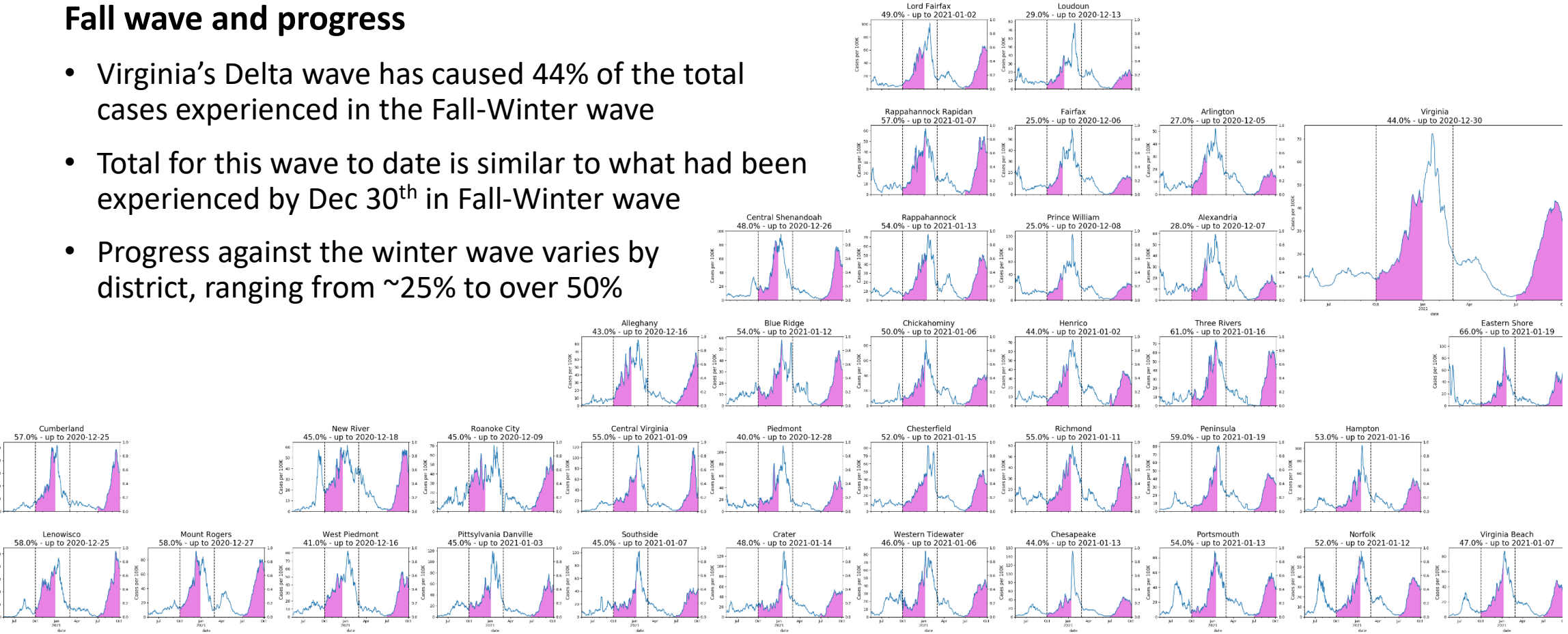
Delta Wave compared to Last Fall – Winter wave

Total cases in Delta wave compared to cases in Fall wave and progress

- Virginia's Delta wave has caused 44% of the total cases experienced in the Fall-Winter wave
- Total for this wave to date is similar to what had been experienced by Dec 30th in Fall-Winter wave
- Progress against the winter wave varies by district, ranging from ~25% to over 50%



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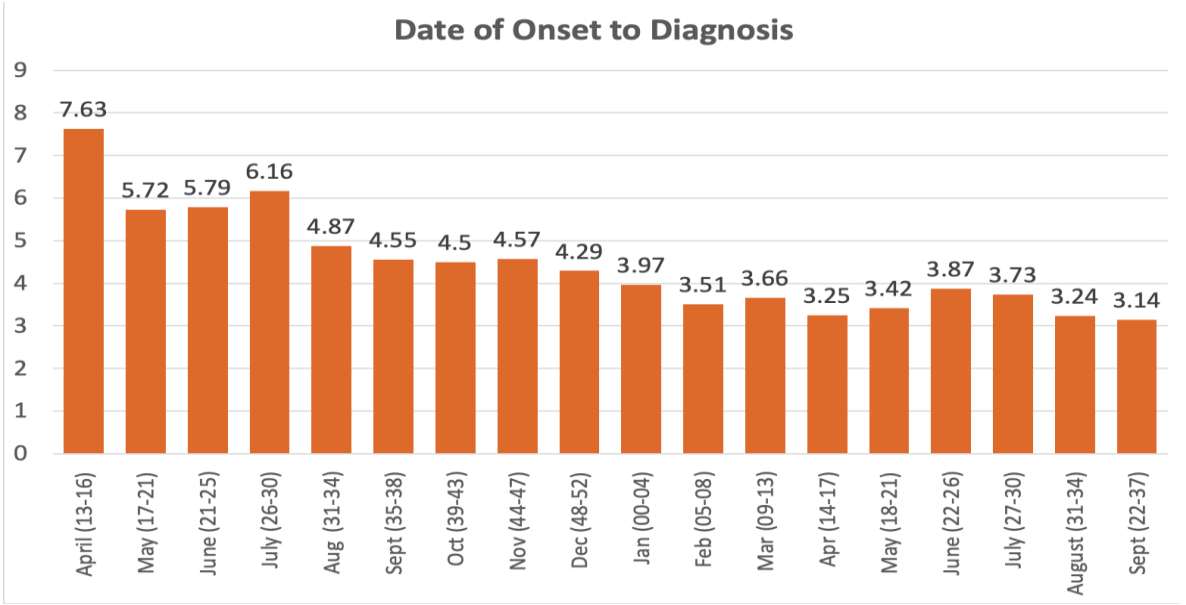
Impact of Delta Wave

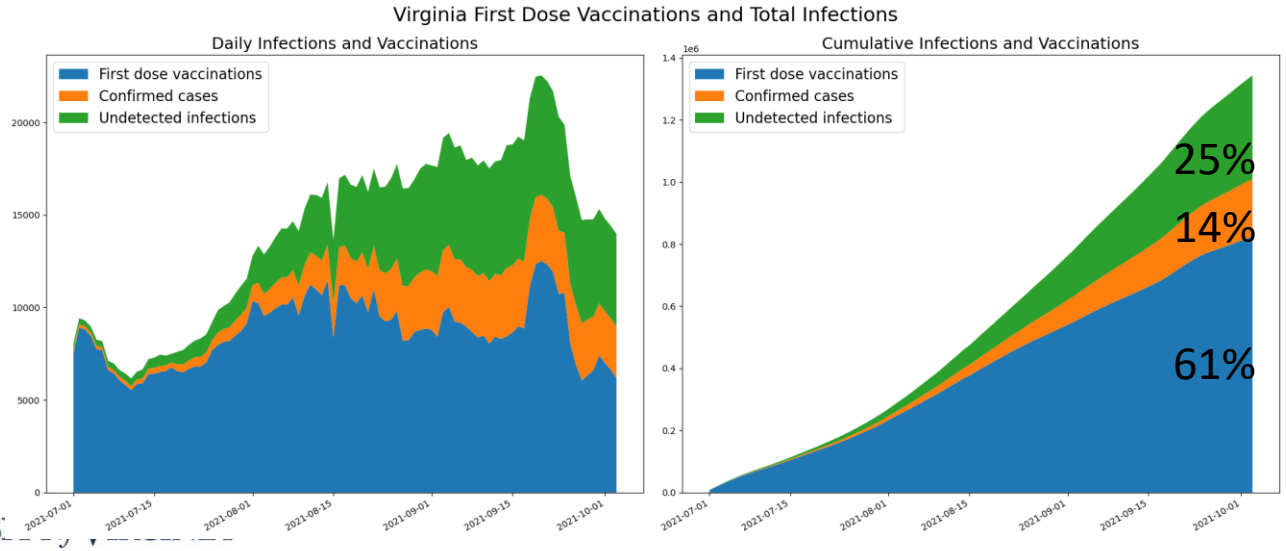
Date of Onset Update

- Time from onset to diagnosis had climbed a little during low case rates in summer but shrunk with delta wave surge



How People have gained immunity

- Since July 1st, count all people vaccinated, confirmed as a case, and estimated to be infected (based on seroprevalence).
- Of people in this group, 61% were vaccinated, 14% had confirmed COVID-19, and 25% were estimated to have been infected (durability of immunity in undetected infections may be more limited)
- Possible overlap with breakthrough infections is limited due to short 3 month time period



Zip code level weekly Case Rate (per 100K)

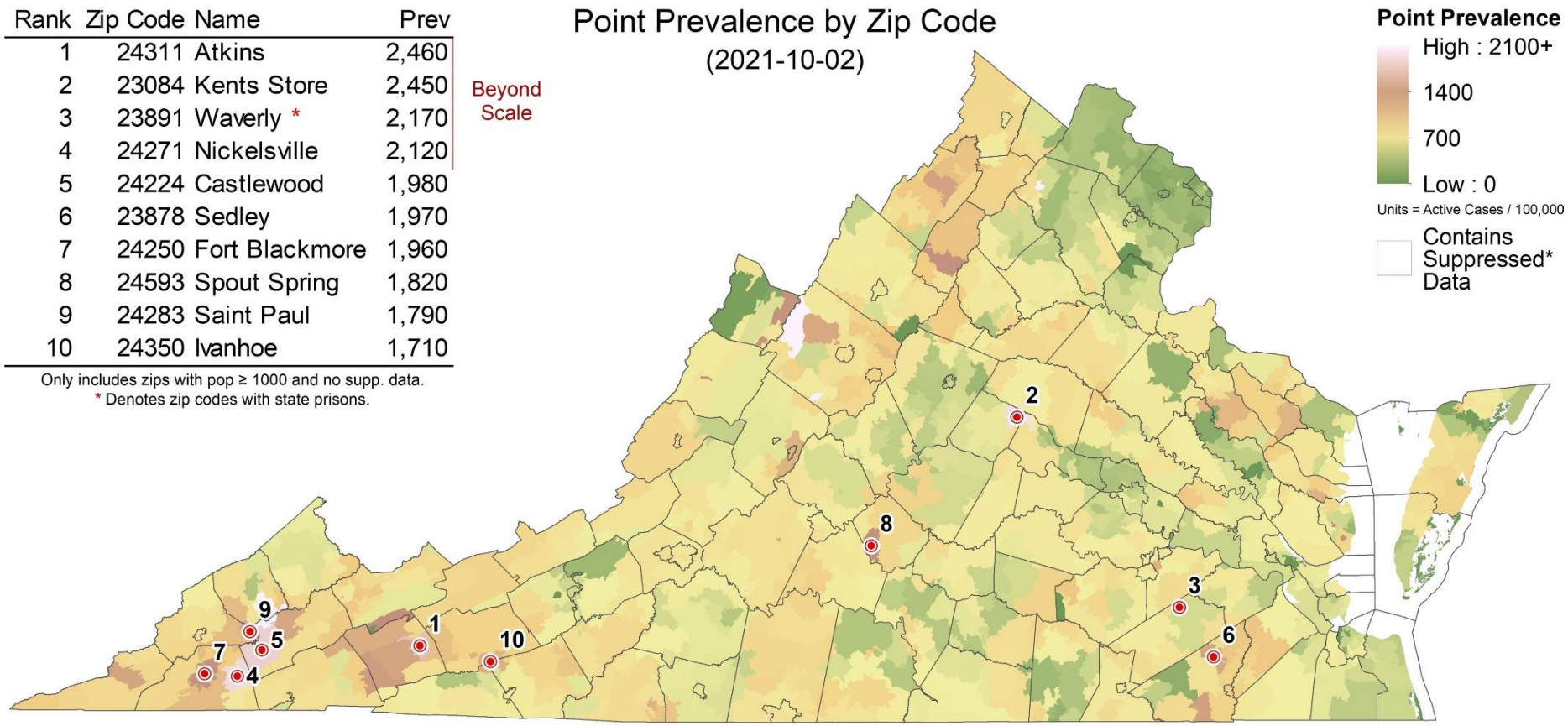
Case Rates in the last week by zip code

- Color scaled adjusted to accommodate the very high prevalence levels this week
- Clusters of high prevalence in Southwest and Eastern
- Some counts are low and suppressed to protect anonymity, those are shown in white

Rank	Zip Code	Name	Prev
1	24311	Atkins	2,460
2	23084	Kents Store	2,450
3	23891	Waverly *	2,170
4	24271	Nickelsville	2,120
5	24224	Castlewood	1,980
6	23878	Sedley	1,970
7	24250	Fort Blackmore	1,960
8	24593	Spout Spring	1,820
9	24283	Saint Paul	1,790
10	24350	Ivanhoe	1,710

Beyond Scale

Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Spatial Empirical Bayes smoothed point prevalence for week ending 2021-10-02.

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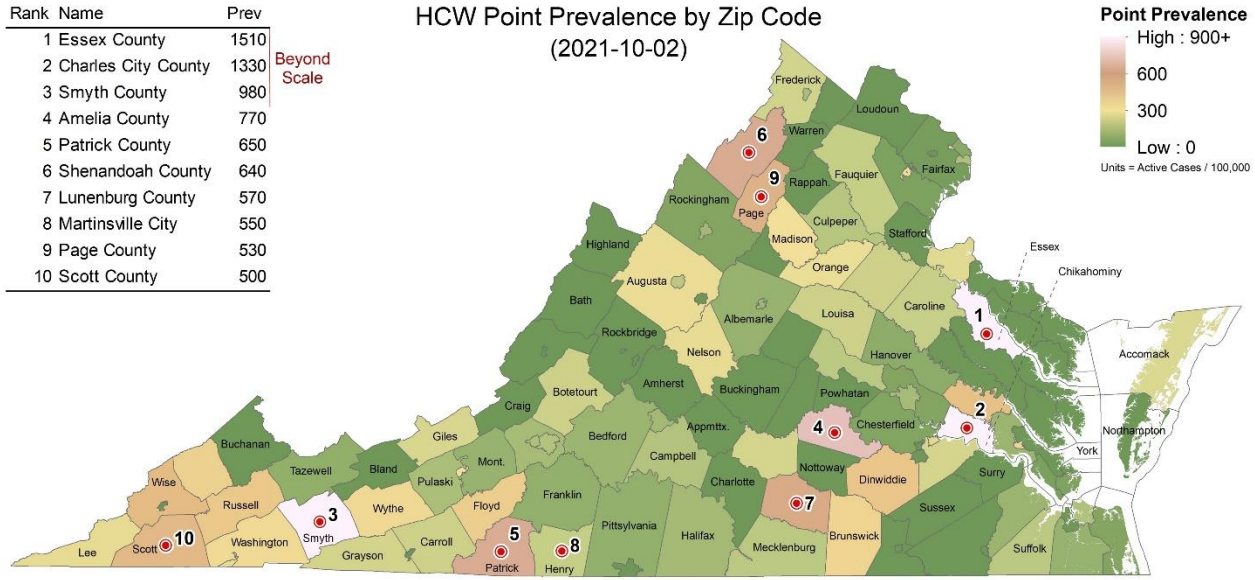
HCW Prevalence

- **HCW prevalence**: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the denominator
  - Clusters of high HCW point prevalence in Franklin City, along the southern border, and far southwest
- **HCW Ratio**: HCW Prevalence / Total Case Prevalence
  - (blue = higher case rate among public, red = higher case rate among HCW)

HCW Prevalence

Rank	Name	Prev
1	Essex County	1510
2	Charles City County	1330
3	Smyth County	980
4	Amelia County	770
5	Patrick County	650
6	Shenandoah County	640
7	Lunenburg County	570
8	Martinsville City	550
9	Page County	530
10	Scott County	500

Beyond Scale

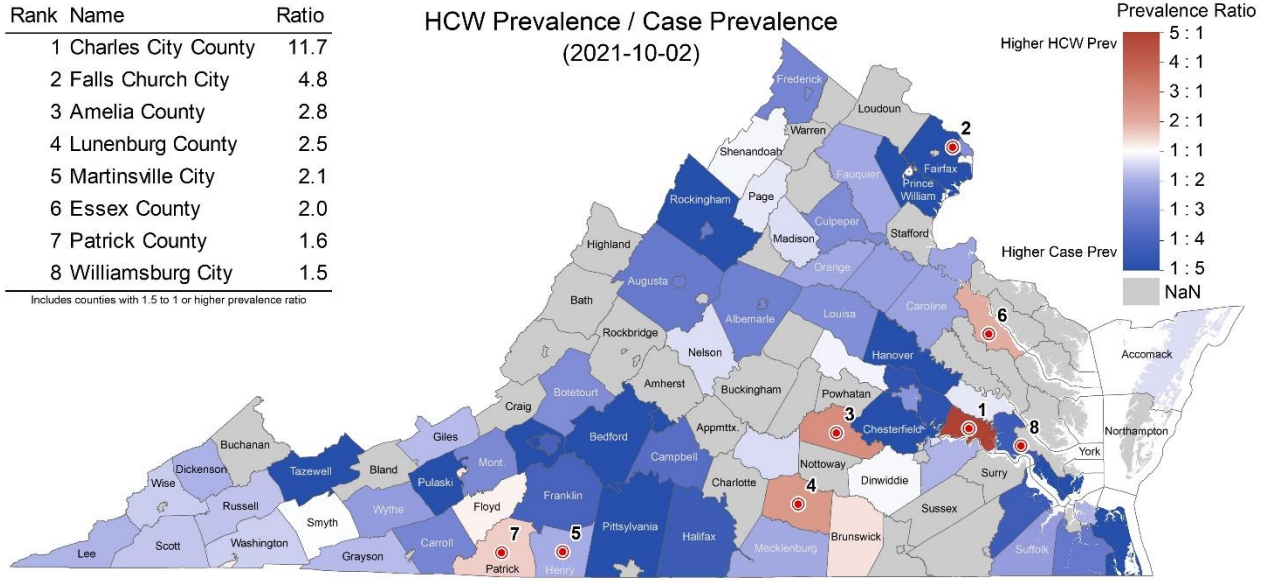


Note: Scale differs from general public prevalence maps.

HCW to Public Prevalence Ratio

Rank	Name	Ratio
1	Charles City County	11.7
2	Falls Church City	4.8
3	Amelia County	2.8
4	Lunenburg County	2.5
5	Martinsville City	2.1
6	Essex County	2.0
7	Patrick County	1.6
8	Williamsburg City	1.5

Includes counties with 1.5 to 1 or higher prevalence ratio



Current Hot-Spots

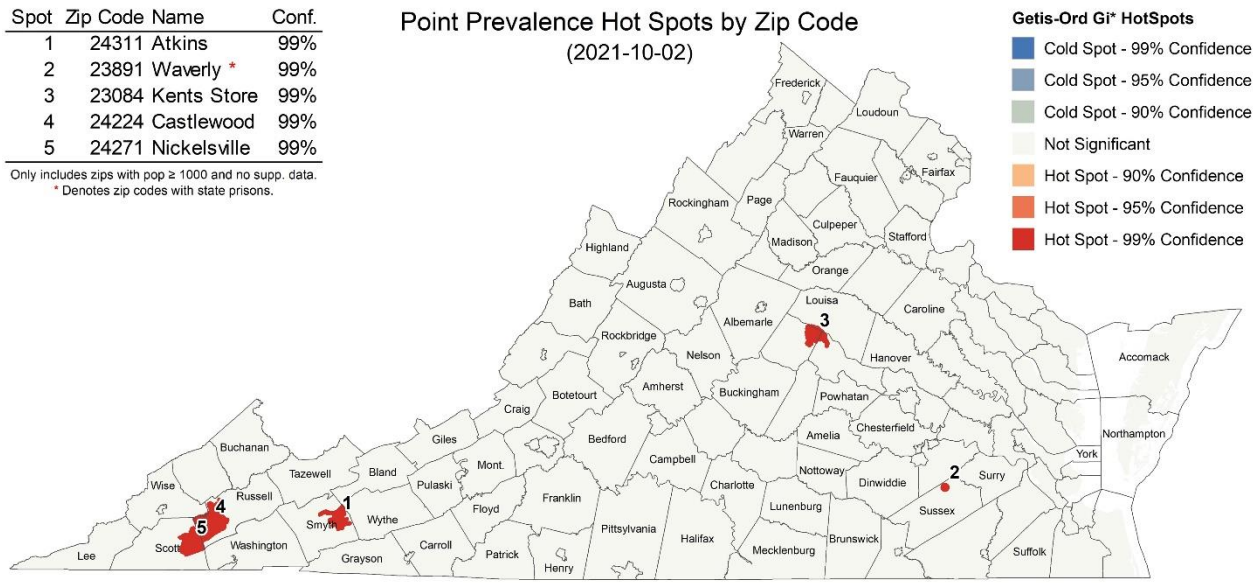
Case rates that are significantly different from neighboring areas or model projections

- **Spatial**: Getis-Ord Gi* based hot spots compare clusters of zip codes with weekly case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The weekly case rate (per 100K) projected last week compared to observed by county, which highlights temporal fluctuations that differ from the model's projections

Spatial Hotspots

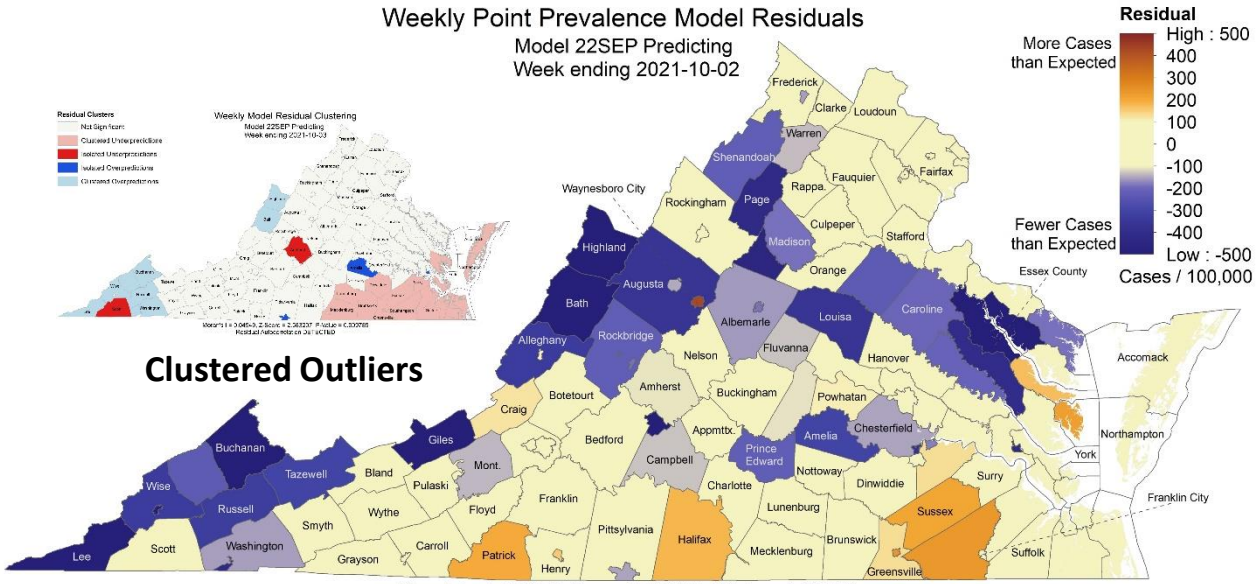
Spot	Zip Code	Name	Conf.
1	24311	Atkins	99%
2	23891	Waverly *	99%
3	23084	Kents Store	99%
4	24224	Castlewood	99%
5	24271	Nickelsville	99%

Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Global Empirical Bayes smoothed point prevalence for week ending 2021-10-02.

Clustered Temporal Hotspots



Moran's I = 0.04949, Z-Score = 2.583207, P-Value = 0.009789
Residual Autocorrelation DETECTED

Model Update – Adaptive Fitting

Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

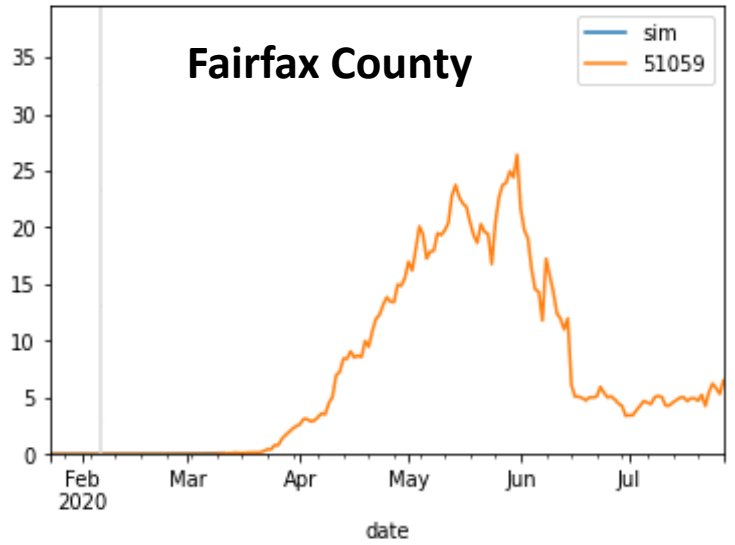
- Allows history to be precisely captured, and used to guide bounds on projections

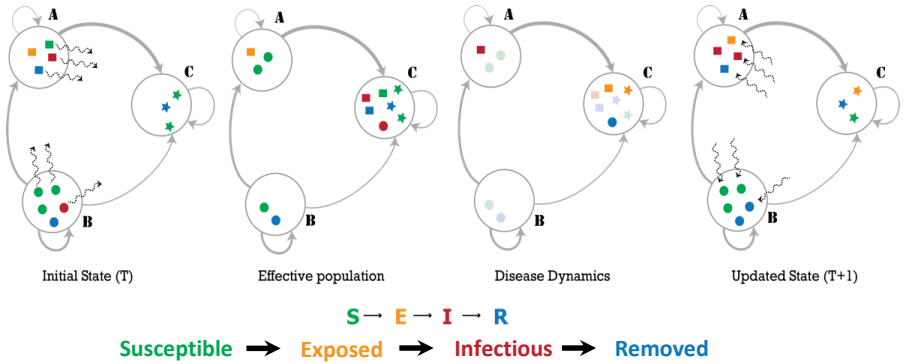
Model: An alternative use of the same meta-population model, PatchSim

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Eliminates connectivity between patches, to allow calibration to capture the increasingly unsynchronized epidemic

External Seeding: Steady low-level importation

- Widespread pandemic eliminates sensitivity to initial conditions
- Uses steady 1 case per 10M population per day external seeding





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Using Ensemble Model to Guide Projections

Ensemble methodology that combines the Adaptive with machine learning and statistical models such as:

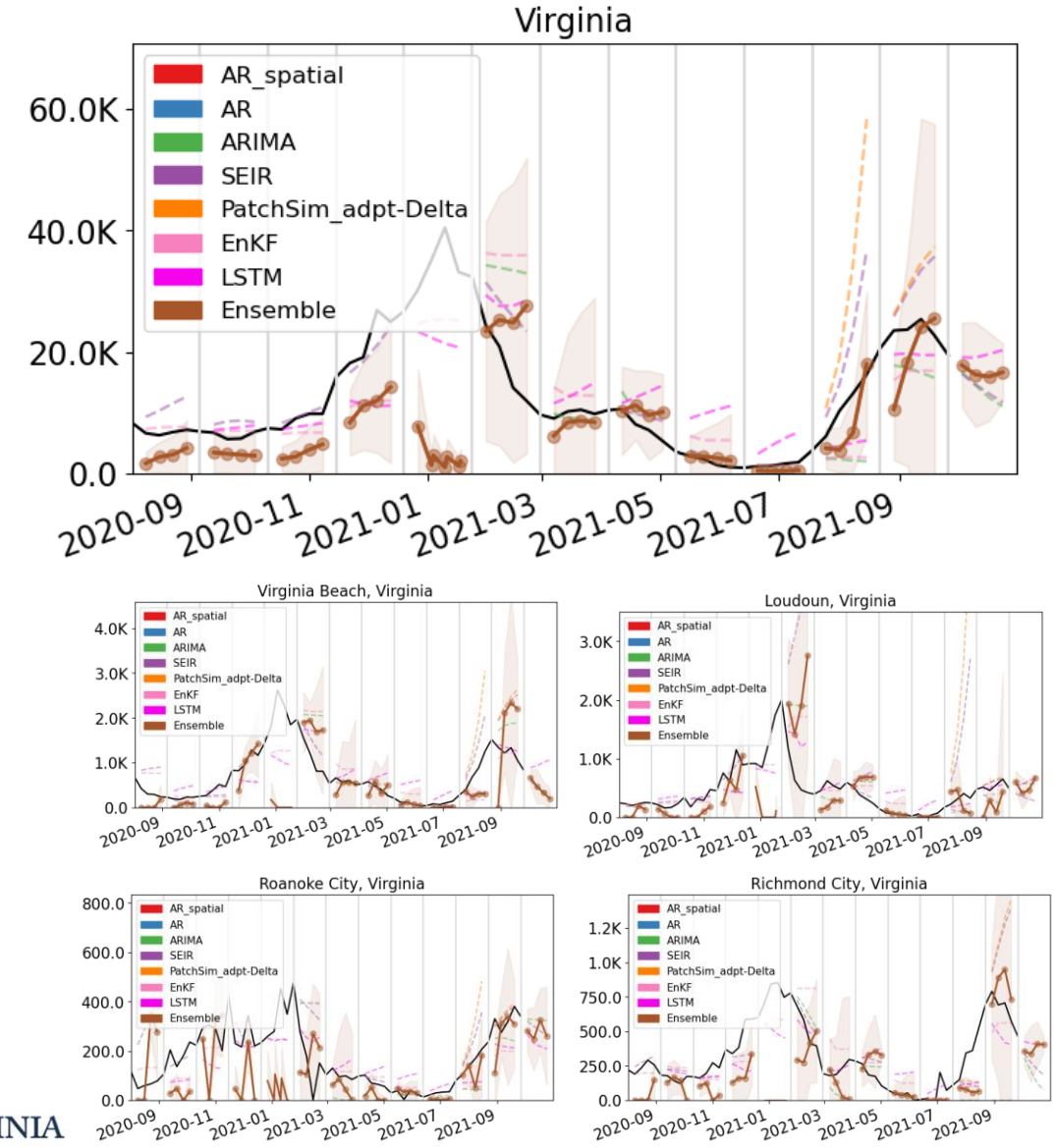
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

<u>Weekly forecasts</u> done at county level.

Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

Ensemble forecast provides additional 'surveillance' for making scenario-based projections.

Also submitted to CDC Forecast Hub.



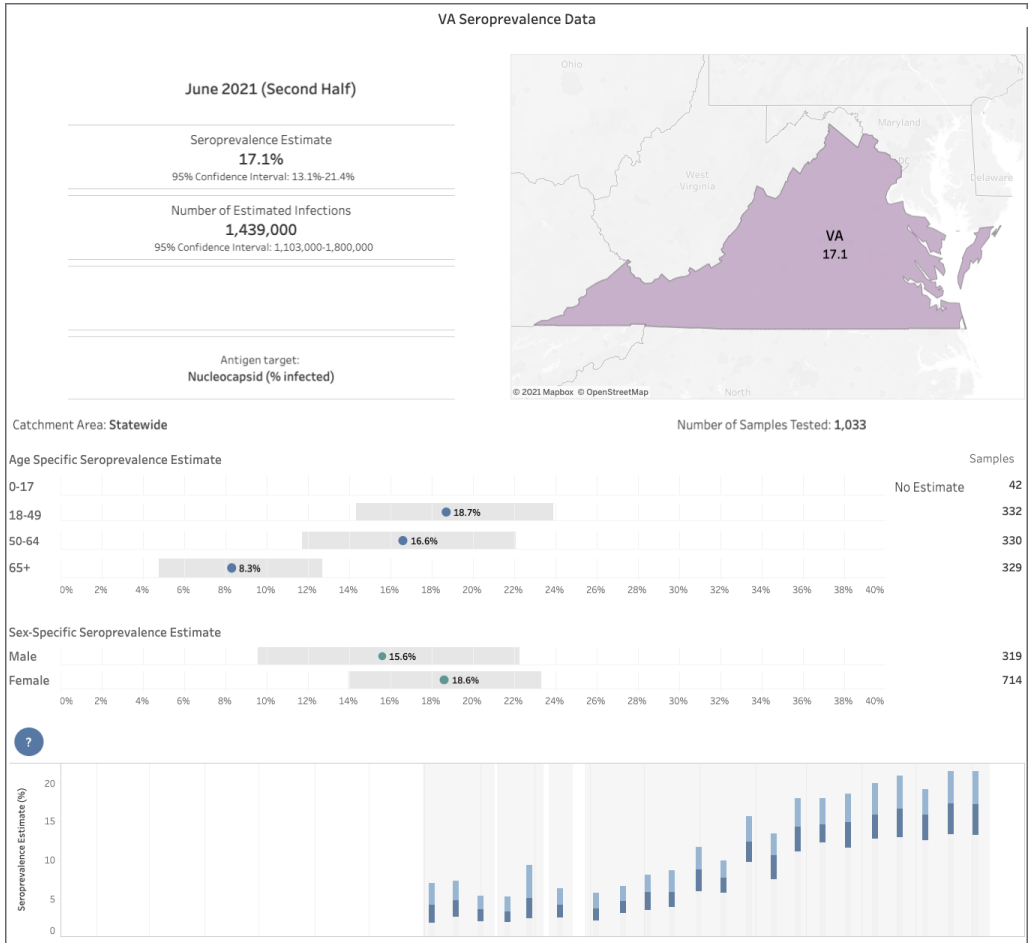
Seroprevalence updates to model design

Several seroprevalence studies provide better picture of how many actual infections have occurred

- CDC Nationwide Commercial Laboratory Seroprevalence Survey

These findings are equivalent to an ascertainment ratio of ~2x in the future, with bounds of (1.3x to 3x)

- Thus for 2x there are 2 total infections in the population for every confirmed case recently
- This measure now fully tracks the estimated ascertainment over time
- Uncertainty design has been shifted to these bounds (previously higher ascertainments as was consistent earlier in the pandemic were being used)



https://covid.cdc.gov/covid-data-tracker/#national-lab

Calibration Approach

- **Data:**
  - County level case counts by date of onset (from VDH)
  - Confirmed cases for model fitting
- **Calibration:** fit model to observed data and ensemble's forecast
  - Tune transmissibility across ranges of:
    - Duration of incubation (5-9 days), infectiousness (3-7 days)
    - Undocumented case rate (1x to 7x) guided by seroprevalence studies
    - Detection delay: exposure to confirmation (4-12 days)
  - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- **Project:** future cases and outcomes generated using the collection of fit models run into the future
  - **Mean trend from last 7 days of observed cases and first week of ensemble's forecast used**
  - Outliers removed based on variances in the previous 3 weeks
  - 2 week interpolation to smooth transitions in rapidly changing trajectories
- **Outcomes**: Data driven by shift and ratio that has least error in last month of observations
  - Hospitalizations: 3 days from confirmation, 6.8% of cases hospitalized
  - Deaths: 11 days from confirmation, 1.45% of cases die

VIRGINIA'S HEALTH IS IN OUR HANDS. Do your part, stop the spread.

COVID-19 in Virginia:

VDH VIRGINIA DEPARTMENT OF HEALTH

Dashboard Updated: 9/28/2021
Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases*	Total Hospitalizations**	Total Deaths
860,493	36,450	12,647
(New Cases: 2,641)^		

Confirmed†	Probable†	Confirmed†	Probable†	Confirmed†	Probable†
644,499	215,994	34,443	2,007	10,674	1,973

* Includes both people with a positive test (Confirmed), and symptomatic with a known exposure to COVID-19 (Probable).
** Hospitalization of a case is captured at the time VDH performs case investigation. This underrepresents the total number of hospitalizations in Virginia.
^New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.
† VDH adopted the updated CDC COVID-19 2021 Surveillance Case Definition on September 1, 2021 which is found here: -- https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2021/

Outbreaks

Total Outbreaks*	Outbreak Associated Cases
4,512	84,773

* At least two (2) lab confirmed cases are required to classify an outbreak.

Testing (PCR Only)

Testing Encounters PCR Only*	Current 7-Day Positivity Rate PCR Only**
9,249,079	9.1%

* PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing."
** Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data.

Multisystem Inflammatory Syndrome in Children

Total Cases*	Total Deaths
85	0

*Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

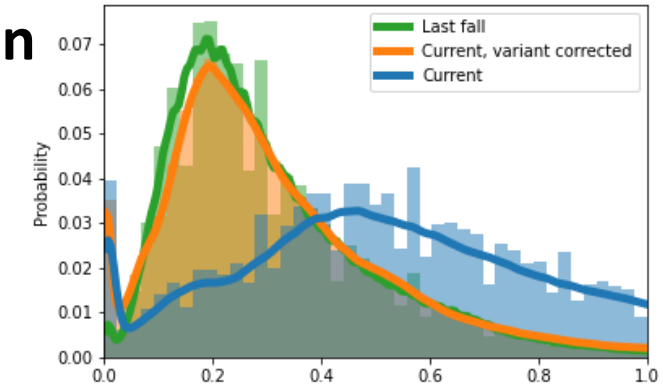
Accessed 8:30am September 29, 2021
https://www.vdh.virginia.gov/coronavirus/

Scenarios – Transmission Conditions

- Variety of factors continue to drive transmission rates
  - Seasonal impact of weather patterns, travel and gatherings, fatigue and premature relaxation of infection control practices
- **Waning Immunity**: Mean of one year protection (rate of 0.0027) similar to Pfizer study
- **Projection Scenarios**:
  - **Adaptive:** Control remains as is currently experienced into the future with assumption that Delta remains as the majority strain
  - **Adaptive-FallWinter2020:** Starting this week the core drivers of transmission from Sept 2020 – Feb 2021 are coarsely replayed but boosted to account for Delta's increased transmissibility
  - **Adaptive-Surge Control:** Starting in one week behaviors and mitigation efforts ramp up over a 2-week period culminating in a 25% reduction in transmission

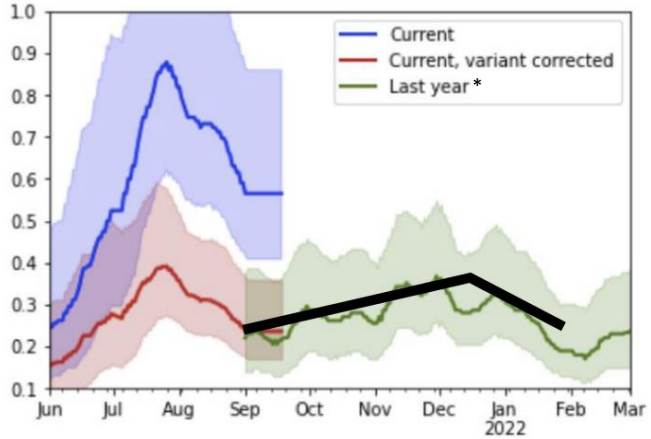
Scenarios – FallWinter2020 Description

September 2020 – February 2021 saw a strong wave of transmission

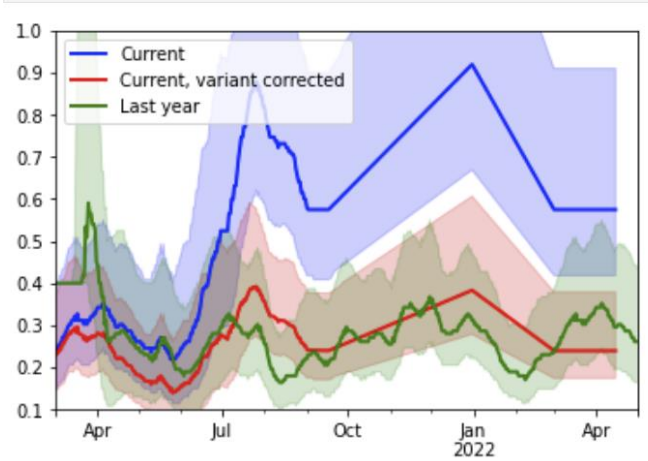


- We analyze previous Fall-Winter's wave vs. current Delta driven wave and observe surprising similarities
  - The distribution of fitted model transmissibility is nearly identical between these periods when corrected for Delta's increased transmissibility
- **FallWinter2020** tries to capture the "transmission drivers" from the past and use them as if they were to occur again this season but with Delta variant (compared to ancestral)
  - Use the above analysis of fitted model transmissibilities from Sept 2020 – Feb 2021 to guide the future transmissibility from Sept 2021 through Feb 2022, but add the enhanced transmissibility of Delta back in

Fitting:
Black line represents the coarsely fitted base transmissibility



* "Last year" is transplanted into 2021-22



Delta enhanced:
Blue trajectory represents current fitted and then projected transmissibility in FallWinter2020

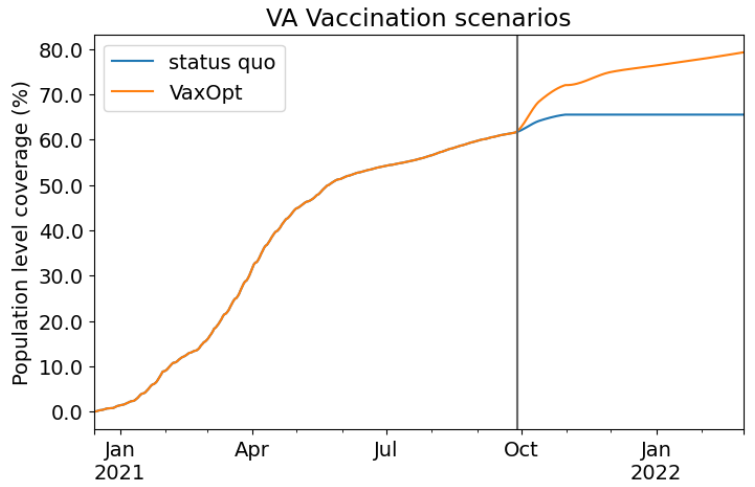
Scenarios – Vaccination Conditions

Vaccine Characteristics

- **Pfizer/Moderna**: 50% after first dose, 95% after second dose (3.5 week gap) **J & J** : 67% efficacy after first dose
- Delay to efficacy from doses is 14 days, immunity lasts at least 7m (NEJM study)

Vaccine Administration Scenarios

- **Status quo (no label):** COVIDcast corrected acceptance estimates (statewide mean is ~80% adults, 65% of population) reached by end of October.
- **Optimistic (VaxOpt):** Expand VA mean acceptance to include ”probably not” (~85% adults) with addition of childhood (5-11 yo) rollout starting in Nov 1st. This follows the same rates as observed of adolescents and results in a net increase of ~10% of population by end of February. Additionally, all counties guaranteed to reach a minimum of 65%, max of 95% by end of October
- Acceptance at county level = regional acceptance +/- relative current vax
- Front-loaded rollout (two-thirds of the remaining in half the time)



Date	status quo	VaxOpt
12/31/20	110.1K	110.1K
1/31/21	648.9K	648.9K
2/28/21	560.9K	560.9K
3/31/21	1.3M	1.3M
4/30/21	1.2M	1.2M
5/31/21	575.3K	575.3K
6/30/21	242.6K	242.6K
7/31/21	197.8K	197.8K
8/31/21	271.0K	271.0K
9/30/21	195.3K	236.4K
10/31/21	306.1K	821.4K
11/30/21	0	240.6K
12/31/21	0	125.1K
1/31/22	0	123.0K
2/28/22	0	122.8K
3/31/22	0	4.7K

Date	status quo	VaxOpt
12/31/20	110.1K	110.1K
1/31/21	759.0K	759.0K
2/28/21	1.3M	1.3M
3/31/21	2.6M	2.6M
4/30/21	3.8M	3.8M
5/31/21	4.4M	4.4M
6/30/21	4.6M	4.6M
7/31/21	4.8M	4.8M
8/31/21	5.1M	5.1M
9/30/21	5.3M	5.3M
10/31/21	5.6M	6.1M
11/30/21	5.6M	6.4M
12/31/21	5.6M	6.5M
1/31/22	5.6M	6.6M
2/28/22	5.6M	6.8M
3/31/22	5.6M	6.8M

Projection Scenarios – Combined Conditions

Name	Txm Controls	Vax	Description
Adaptive	C	SQ	Likely trajectory based on conditions remaining similar to the current experience
Adaptive-VaxOpt	C	VO	Vaccination through October reaches an optimistically high level of expanded coverage (85%)
Adaptive-SurgeControl	25%	SQ	Transmission rates in the next month reduced through increased control from non-pharmaceutical interventions, with status quo vax and Delta
Adaptive-FallWinter2020	FallWinter 2020	SQ	Transmission rates coarsely follow the rates from last September through this February but are boosted by Delta's enhanced transmissibility
Adaptive-FallWinter2020-VaxOpt	FallWinter 2020	VO	Transmission rates coarsely follow the rates from last September through this February but are boosted by Delta's enhanced transmissibility, with optimistic vax

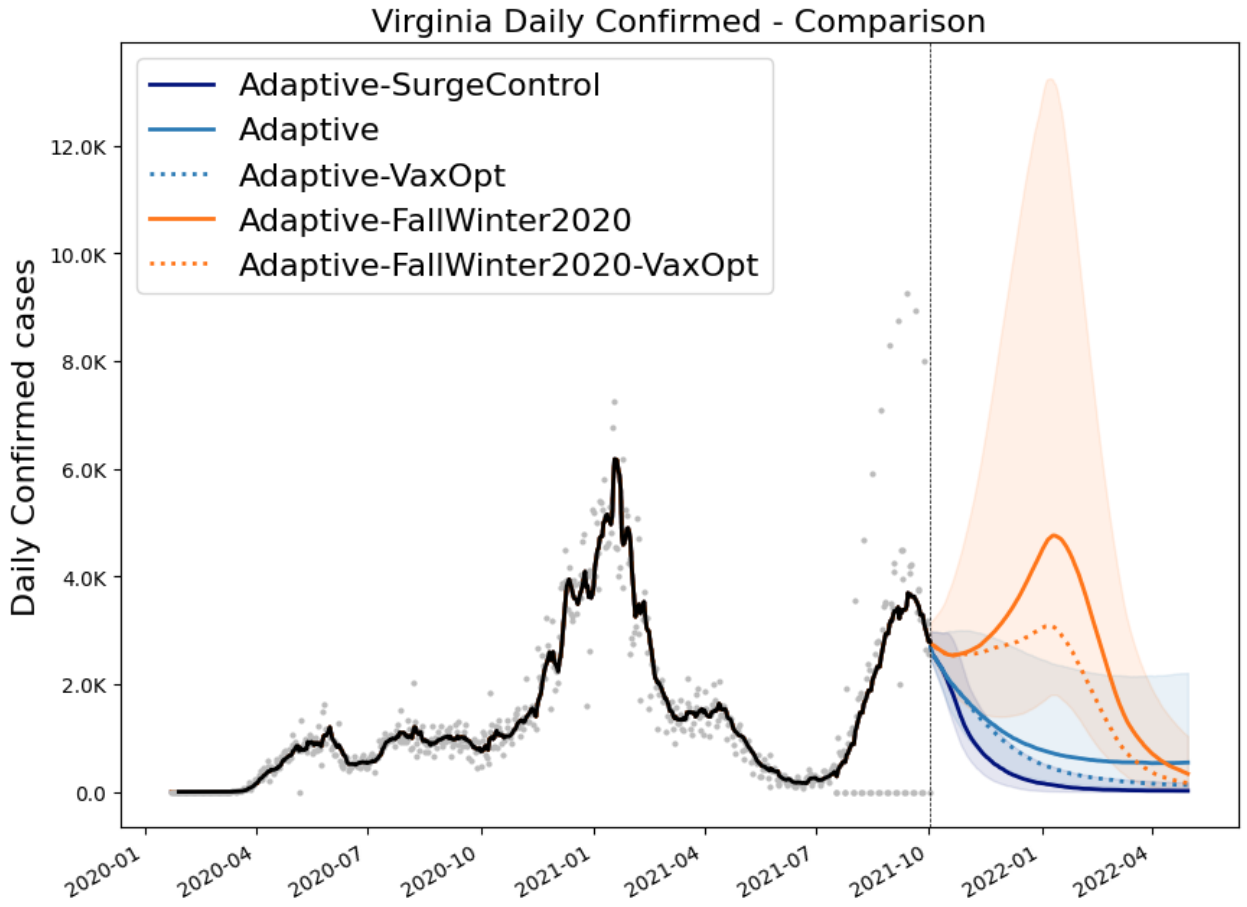
Transmission Controls:
C = Current levels persist into the future
25% = Transmission rates are reduced by 25% with a gradual introduction, concluding in 4 weeks
FallWinter2020 = Transmission rates from Sept 2020 – Feb 2021 are coarsely replayed but boosted by Delta's increased transmissibility

Vaccinations:
SQ = Status quo acceptance leads to low rates of vaccination through the summer
VO = Vaccination acceptance optimistically expands with increased rates through the summer

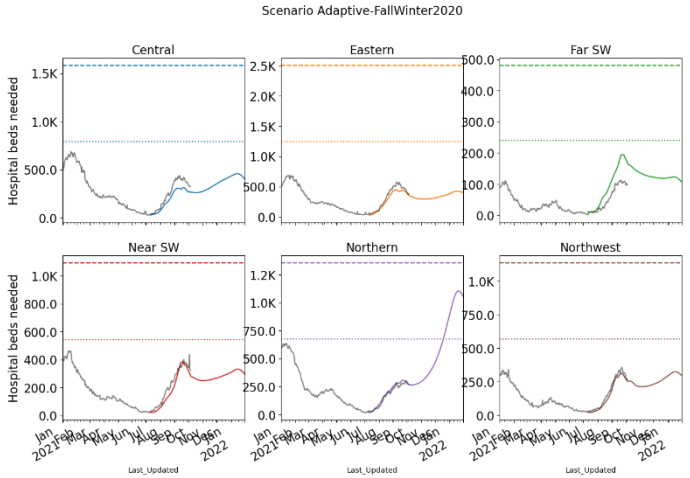
Model Results

Outcome Projections

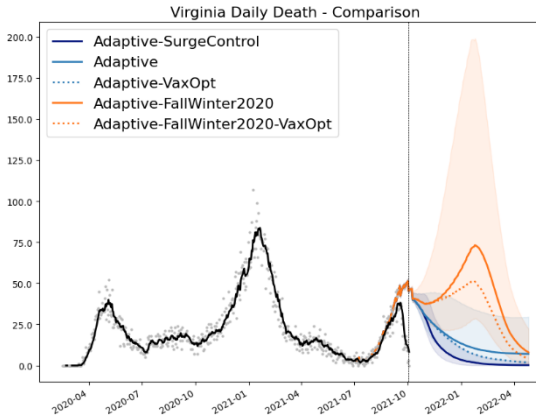
Confirmed cases



Estimated Hospital Occupancy

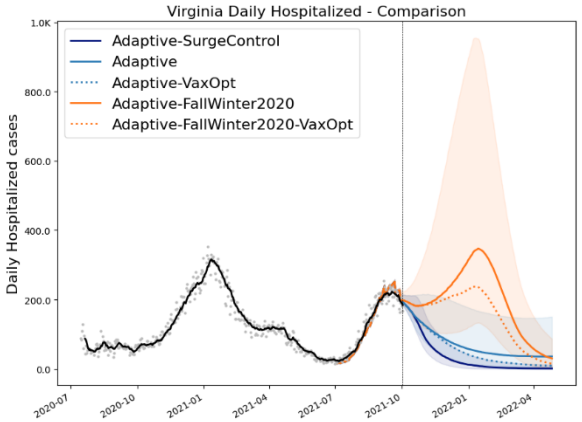


Daily Deaths



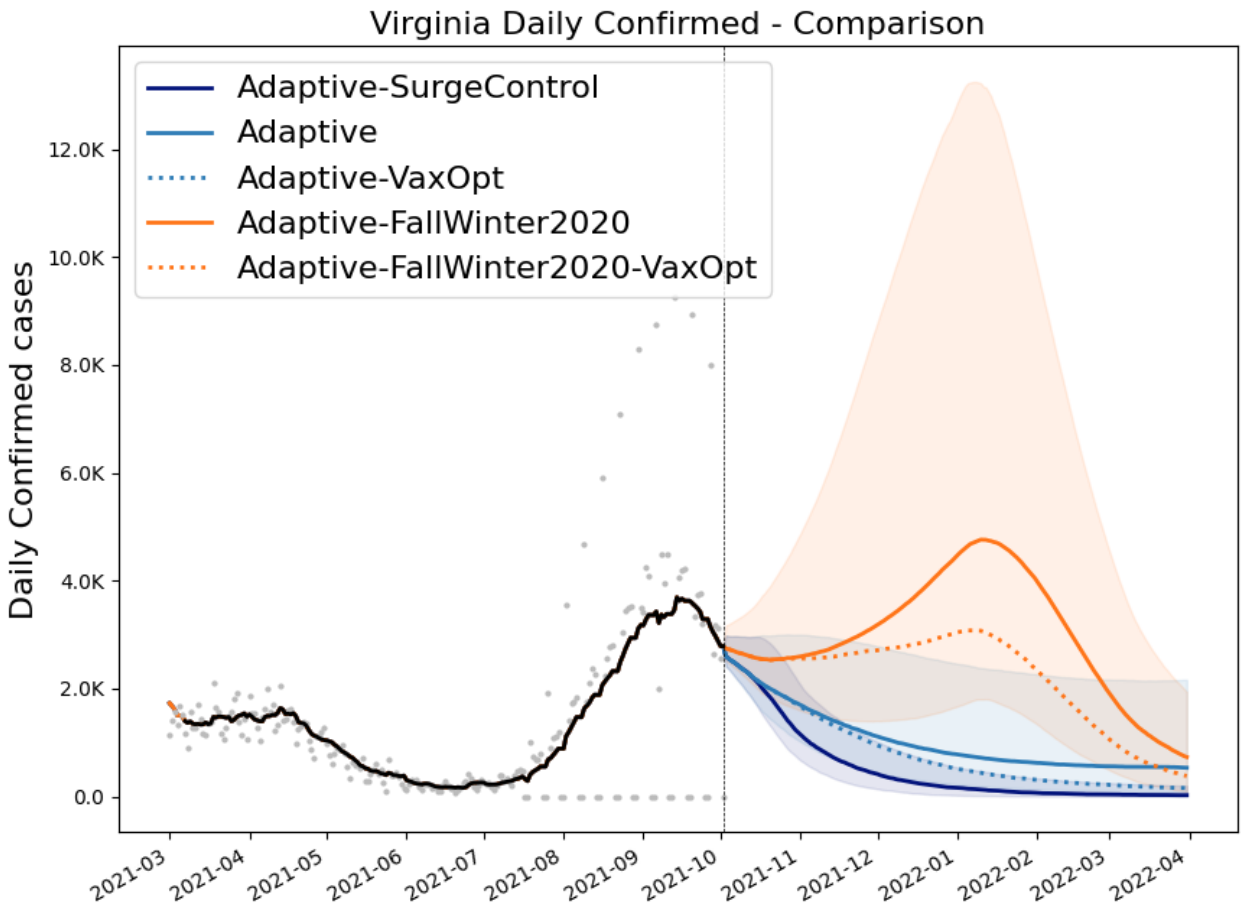
Death ground truth from VDH "Event Date" data, most recent dates are not complete

Daily Hospitalized

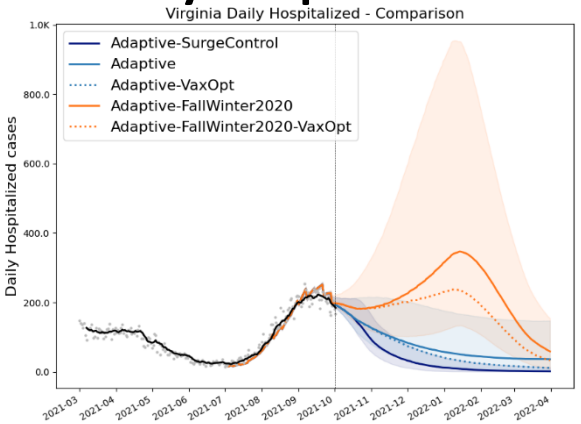


Outcome Projections – Closer Look

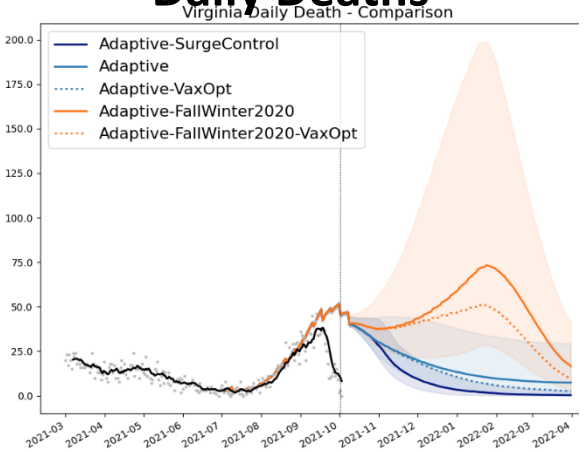
Confirmed cases



Daily Hospitalized



Daily Deaths



Death ground truth from VDH "Event Date" data, most recent dates are not complete

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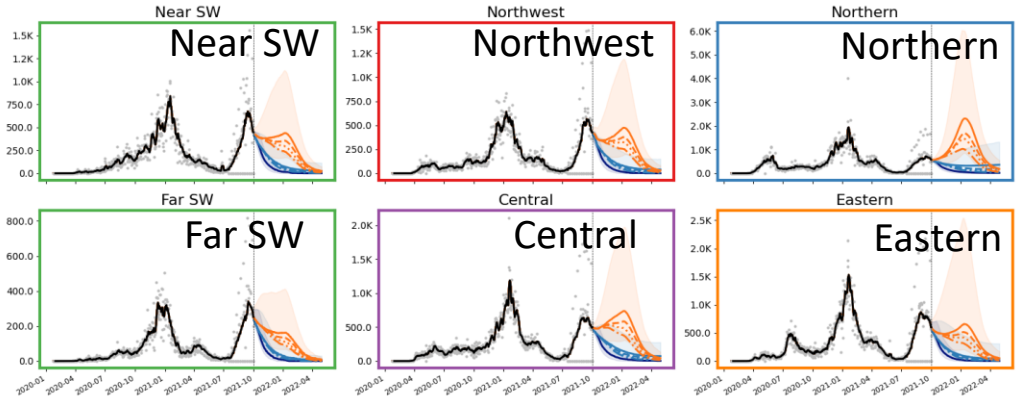
Detailed Projections: All Scenarios

Projections by Region

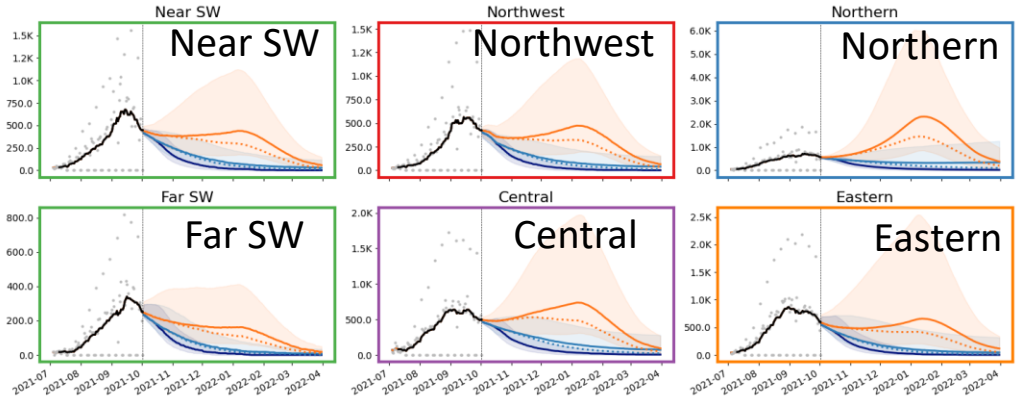


Projections by District

Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

Detailed Projections: All Scenarios - Closer Look

Projections by Region



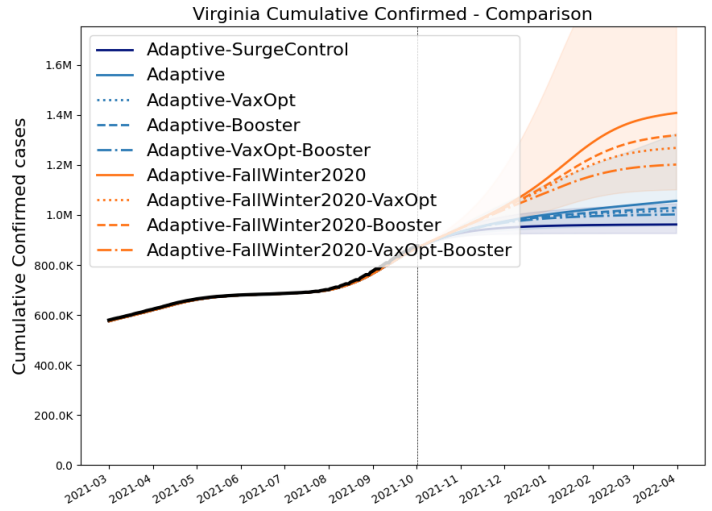
Projections by District

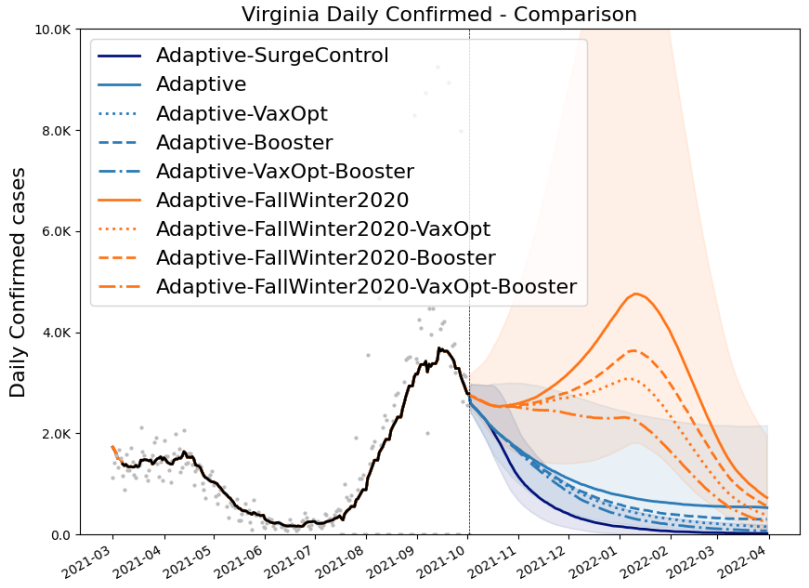
Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

Impact of Expanded Vaccine Coverage & Boosted Immunity

Immunity from Vaccine is expanding, with 3rd doses as well as potential for higher adult coverage & 5-11 year olds potentially becoming eligible soon.

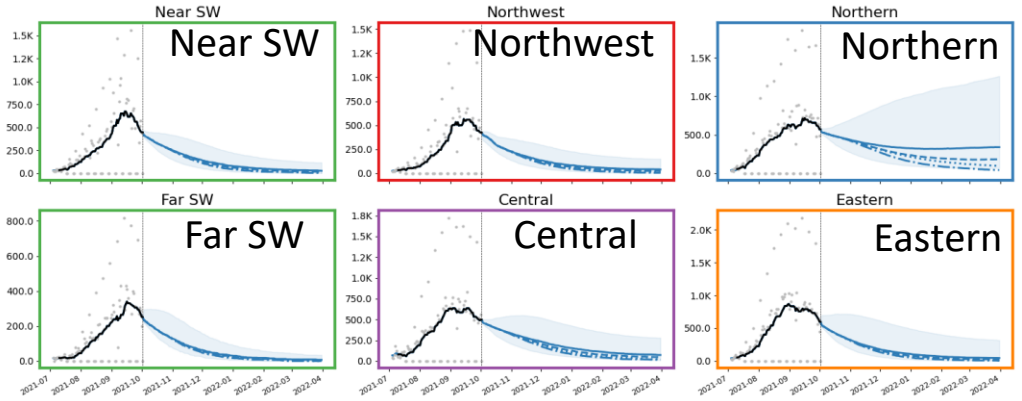
- Model boosters with 50% uptake after 6 months of initial vax, returning waned immunity back to 95% and 5-11 yo becoming eligible Nov 1st
- Third doses may reduce case counts by ~35K, VaxOpt alone by ~50K, and combined ~70K
- When challenged with another FallWinter wave like 2020, the 3rd dose may reduce cases by ~285K, VaxOpt alone by ~340K, and combined by ~410K
- Distribution and uptake of 3rd dose and its full impact on transmission dynamics are not well understood, these estimates are preliminary



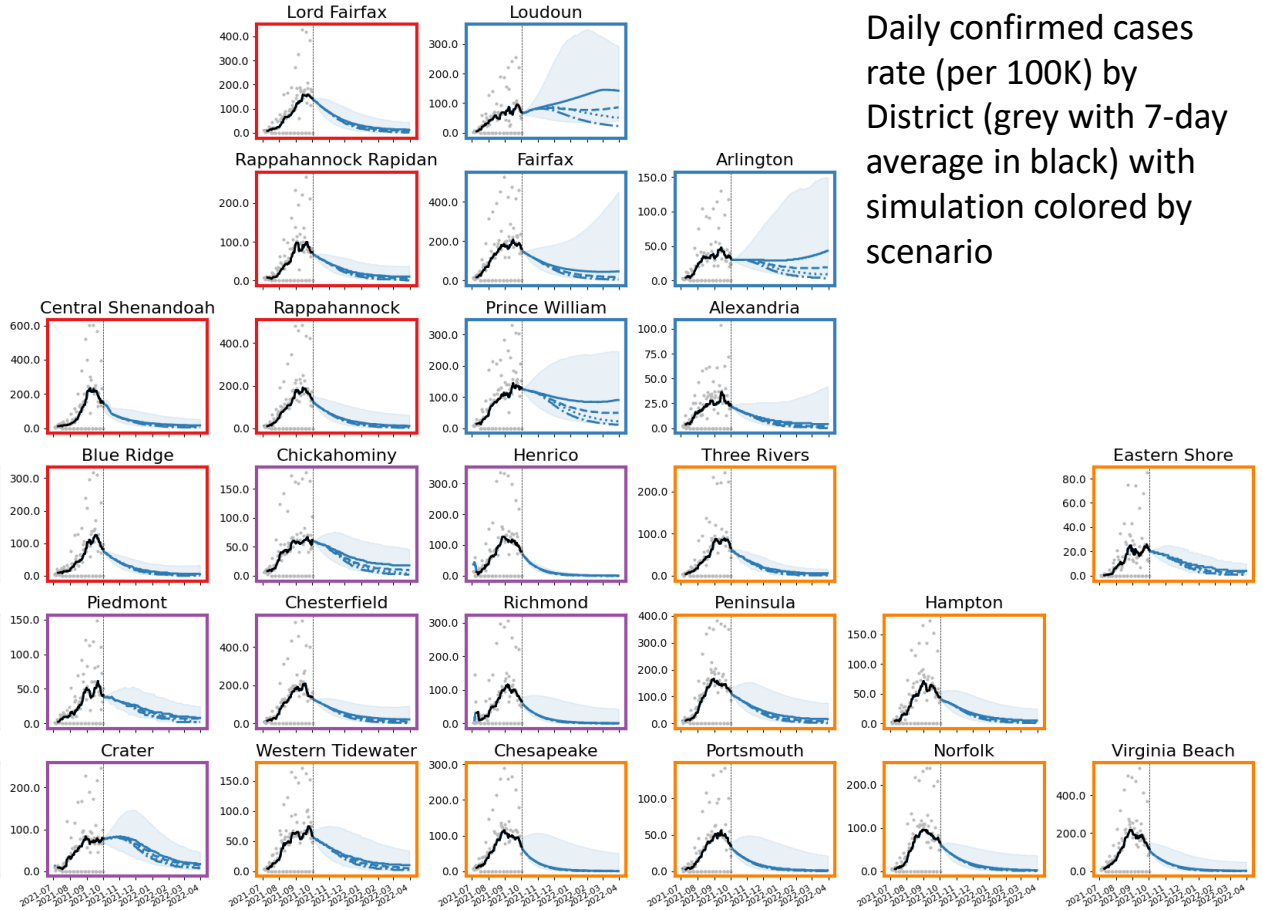


Detailed Projections: Adaptive with Vax Scenarios

Projections by Region



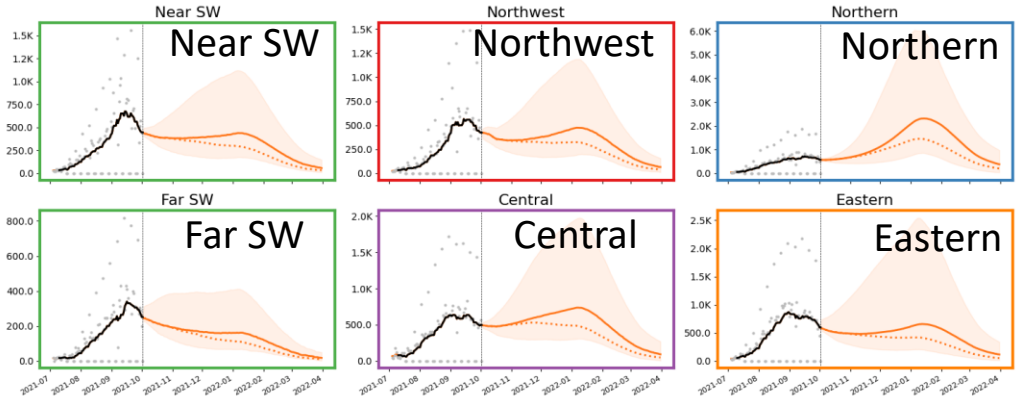
Projections by District



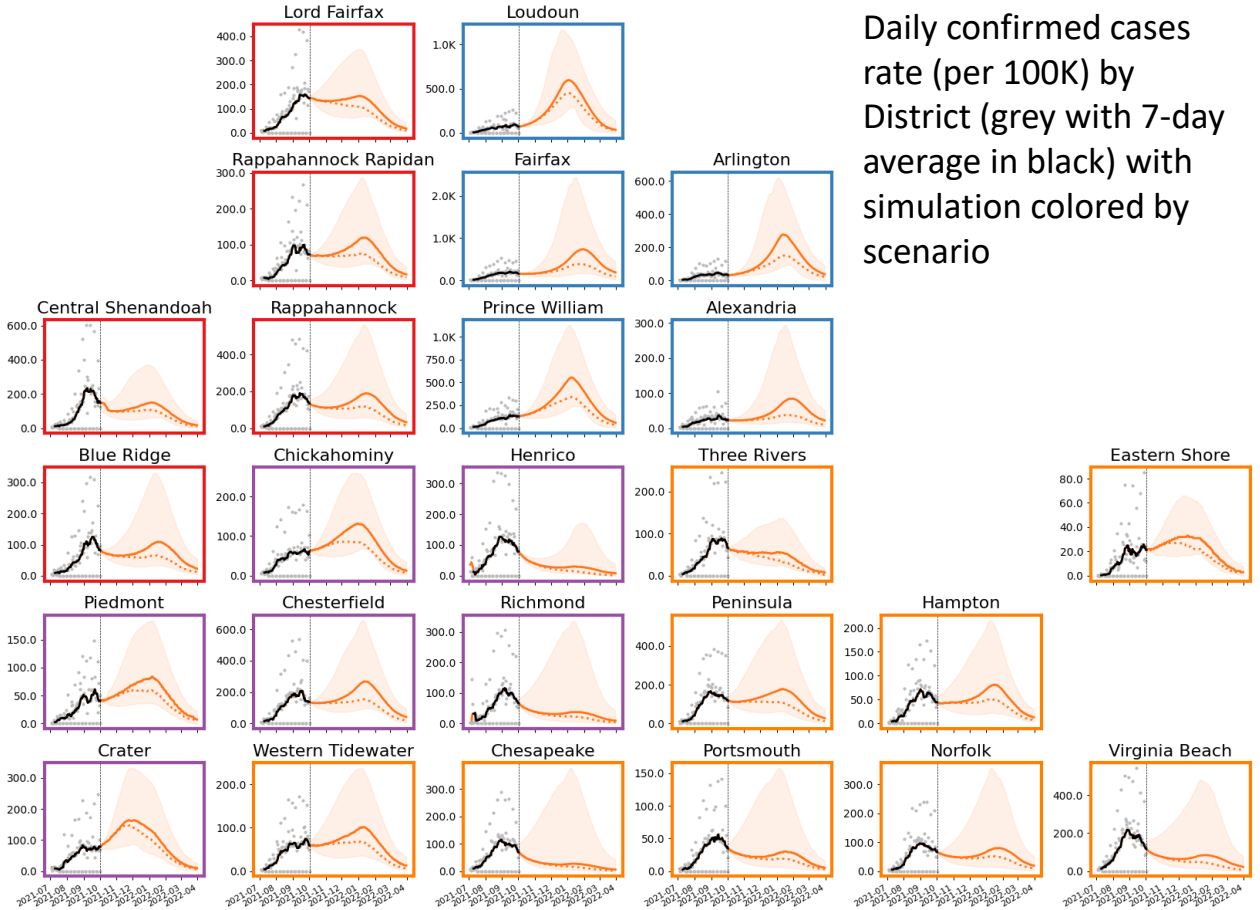
Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

Detailed Projections: Adaptive-FallWinter2020 with Vax Scenarios

Projections by Region



Projections by District

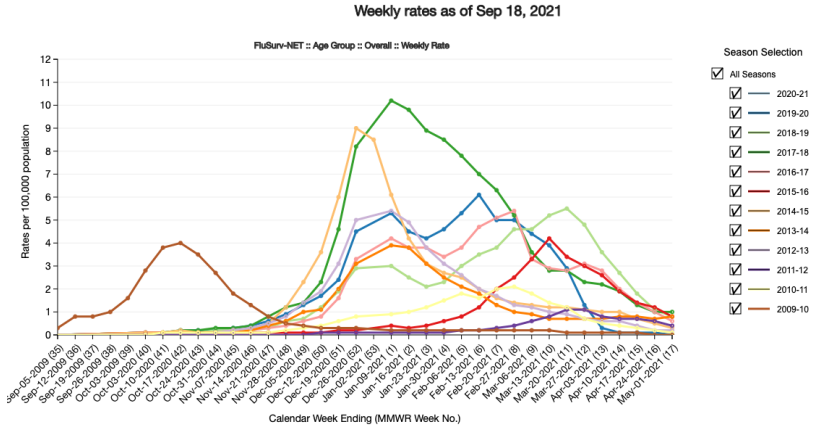


Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

Impact of Influenza based on Previous Intense Flu Seasons

Augment COVID-19 hospitalizations with that of past Influenza seasons

- Include hybrid seasons that use timing of one season but are scaled by severity of another
- Due limited historical data on Virginia flu hospitalizations currently using national rates applied to VA population



https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html

2009-10 – Pandemic 2009 H1N1 season

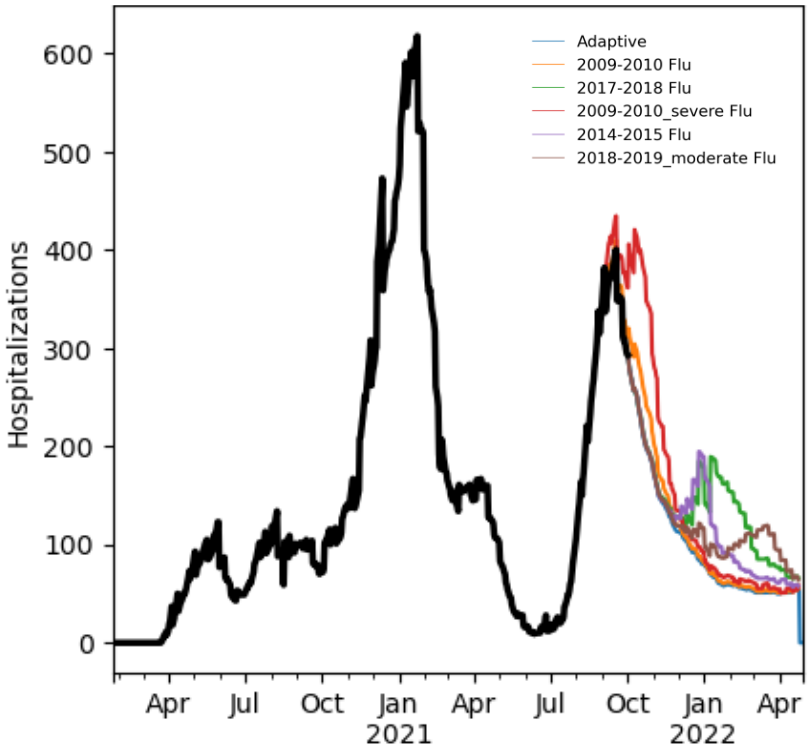
2017-18 – Timing and severity of 2017-18 season

2009-10_severe – Timing of 2009 pandemic (early) with the severity of the 2017-18 season

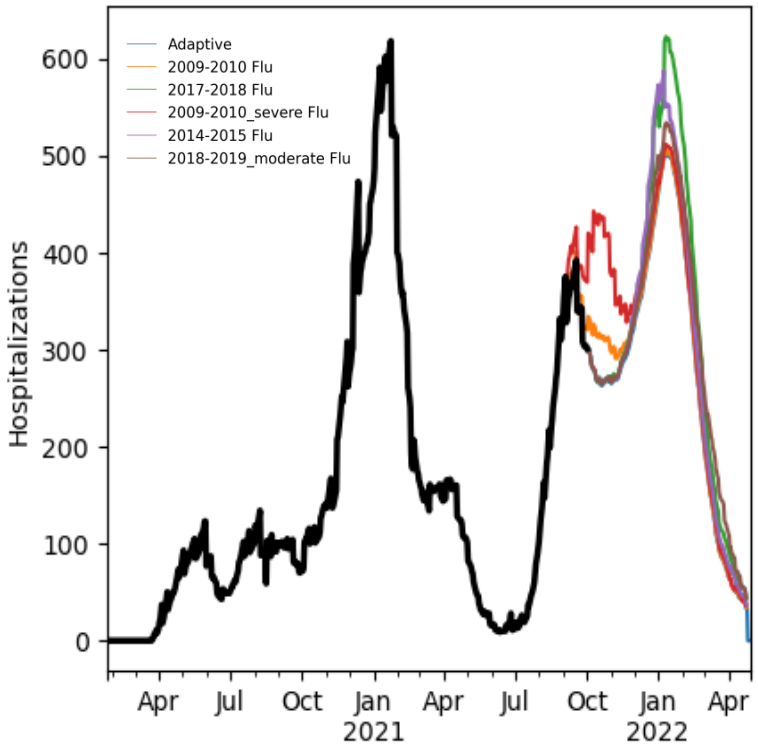
2014-15 – Timing and severity of 2014-15 season

2018-19_moderate – Timing of 2018-19 (late) season with severity of 2014-15

Adaptive



Adaptive – FallWinter2020



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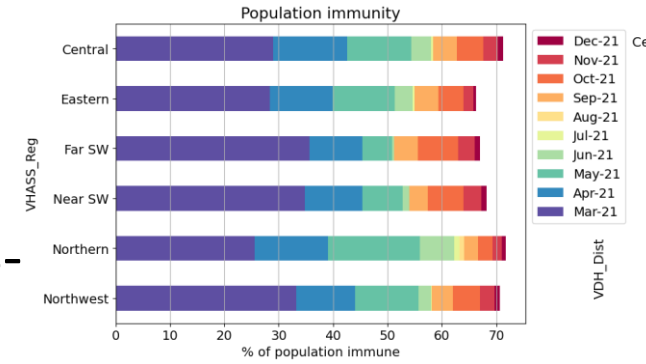
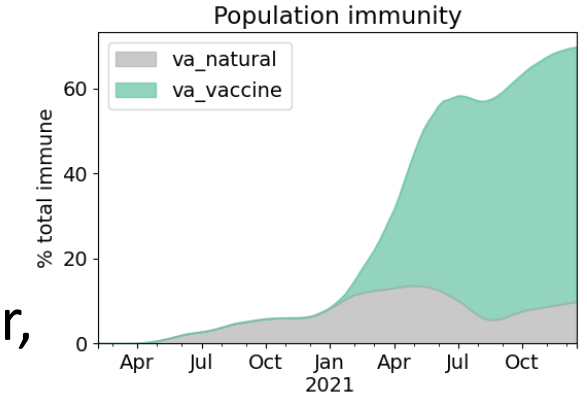
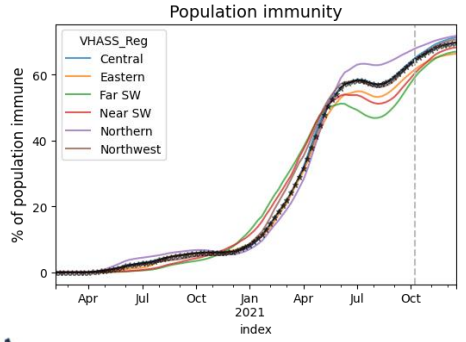
Virginia's Progress on Population Immunity

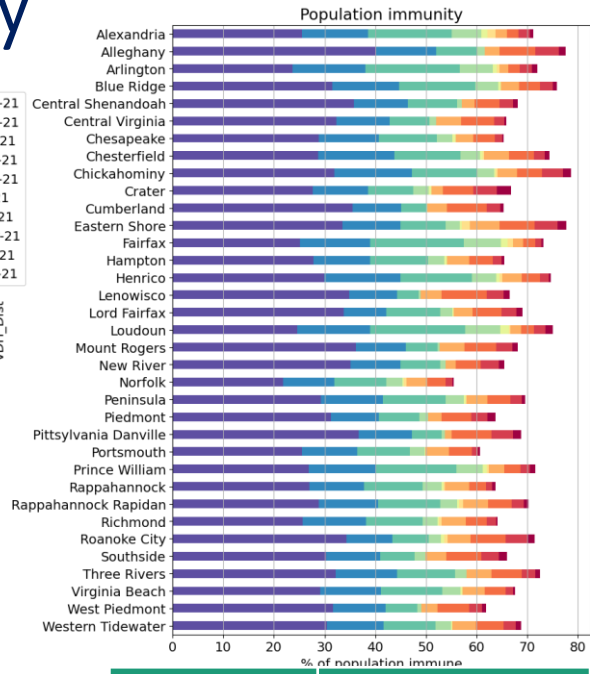
Natural Immunity and Vaccines combine to produce a population level of immunity

- Duration of immunity from infection with SARS-CoV2 still not well understood
  - We assume a conservative 6 month period of protection for these calculations
  - Do **not** factor in variant immune escape
  - Natural immunity is well calibrated to recent seroprevalence surveys
- Vaccine induced immunity is likely to last longer, we assume indefinite protection
  - This also assumes that all administered vaccines remain protective against current and future variants
- Population immunity depends on a very high proportion of the population getting vaccinated
  - Current models track measured seroprevalence









Region	% pop immune (est.)*
Central	64%
Eastern	60%
Far SW	57%
Near SW	59%
Northern	67%
Northwest	63%
Virginia	63%

* As of Oct 3, 2021 for entire population

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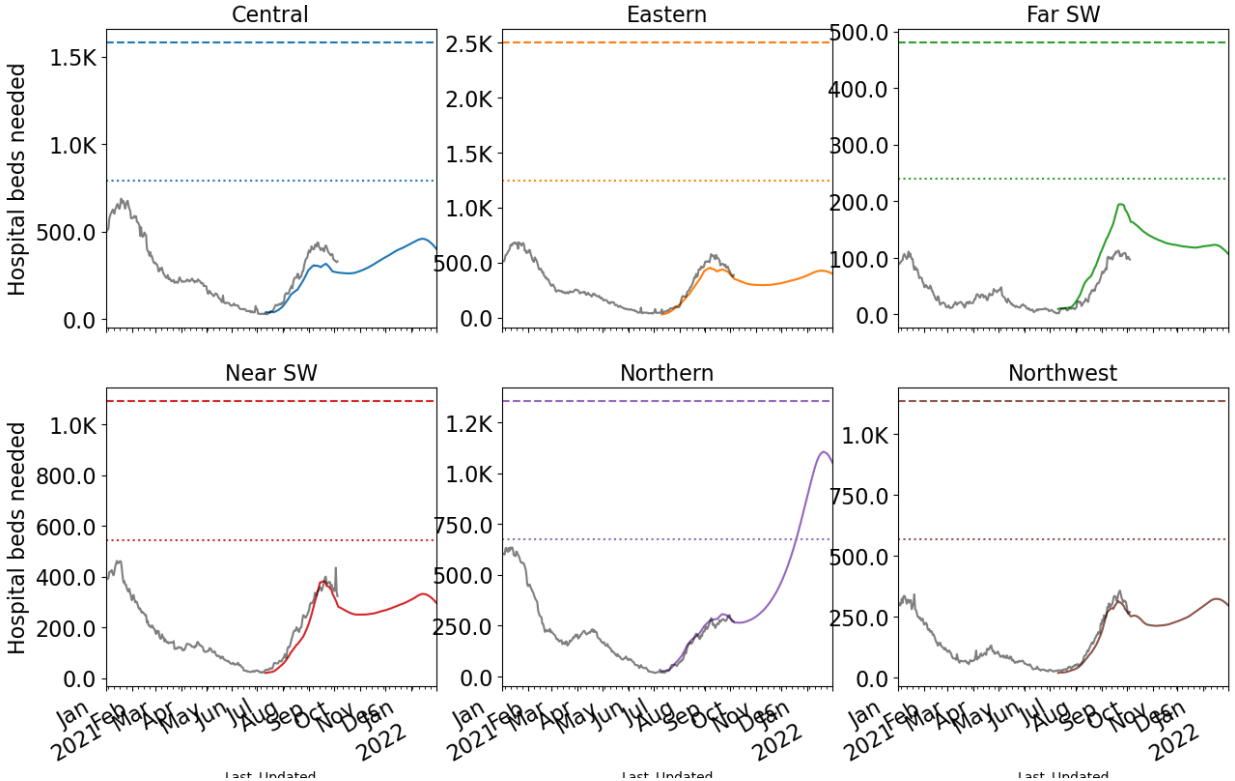
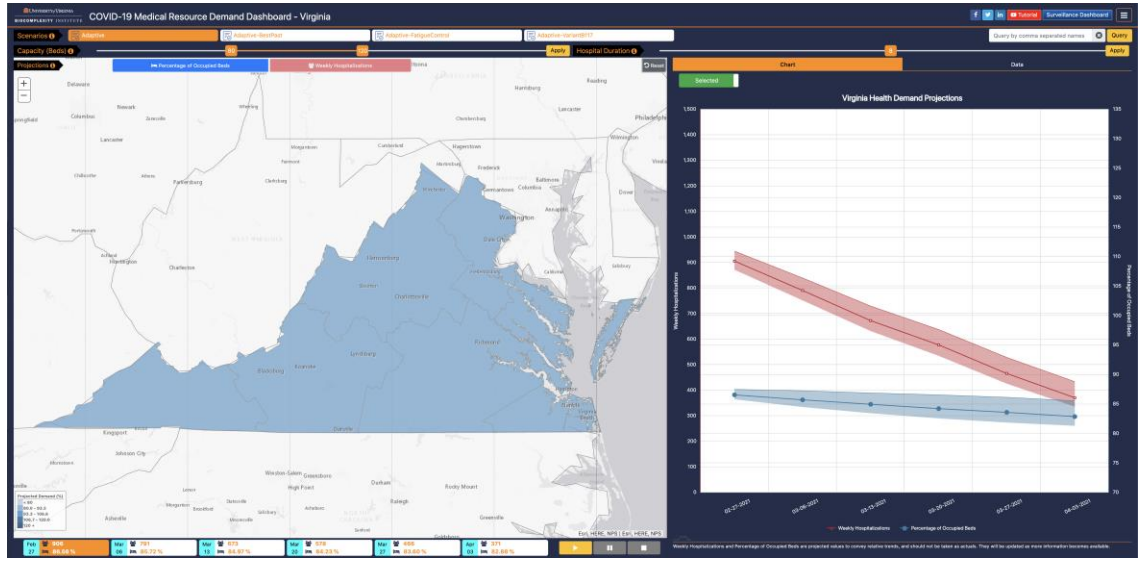
Hospital Demand and Bed Capacity by Region

Capacities* by Region – Adaptive FallWinter2020

COVID-19 capacity ranges from 80% (dots) to 120% (dash) of total beds





https://nssac.bii.virginia.edu/covid-19/vmrddash/

Adaptive FallWinter2020 scenario shows that even with Delta enhanced severity:

- No regions should exceed their surge capacities
- Some regions may exceed initial capacities

* Assumes average length of stay of 8 days

Key Takeaways

Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

- **Case rates in Virginia continue to decline, with nearly all districts declining as well; case rates remain high and the rate of decline remains modest**
- VA 7-day mean daily incidence is slightly down to 32/100K from 35/100K; US is also slightly down to 39/100K (from 43/100K)
- Projections show continued decline, with a few districts showing some growth under current conditions
- Significant future case growth remains possible when tested with transmission drivers from last year
- Recent updates:
  - Analysis to show potential impact of Influenza based on past seasons
  - Prelim analysis of impact of expanded immunity through 3rd doses
  - Adjustment to higher levels of assumed immunity waning (natural and vaccine)

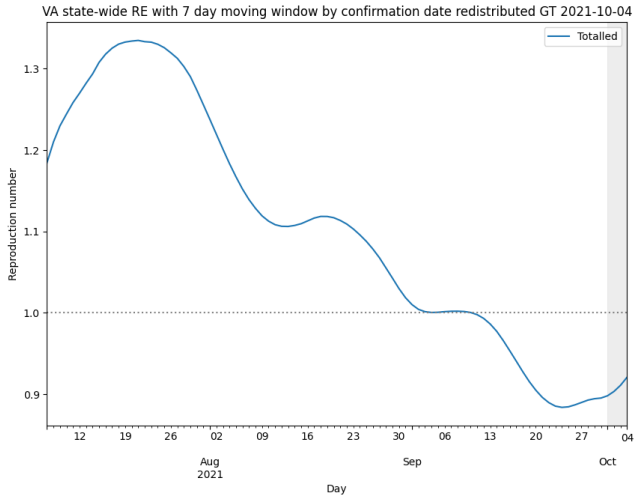
The situation continues to change. Models continue to be updated regularly.

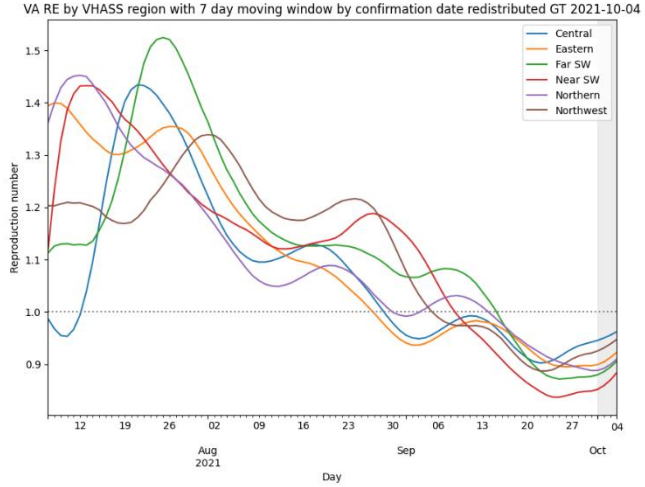
Additional Analyses

Estimating Daily Reproductive Number –
Redistributed weekend gap

Oct 5th Estimates

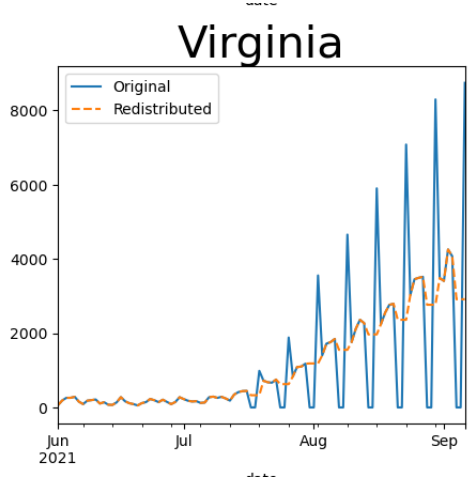
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.851	0.000
Central	0.904	0.008
Eastern	0.891	0.015
Far SW	0.827	-0.001
Near SW	0.798	-0.001
Northern	0.840	-0.011
Northwest	0.885	0.014





Skipping Weekend Reports biases estimates

Redistributed Monday to fill in weekend, and then estimate R from ”smoothed” time series



Methodology

- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Weekly Cases and Hospitalizations

Weekly confirmed cases

Week Ending	Adaptive	Adaptive-VaxOpt	Adaptive-SurgeControl	Adaptive-FallWinter 2020	Adaptive-FallWinter 2020-VaxOpt
10/3/21	20216	20215	20215	20361	20361
10/10/21	17169	17154	17173	18770	18779
10/17/21	15388	15358	15207	18047	18052
10/24/21	13835	13799	12496	17783	17768
10/31/21	12556	12458	9488	17969	17865
11/7/21	11343	11052	7171	18375	17916
11/14/21	10240	9706	5601	18994	18054
11/21/21	9286	8564	4412	19963	18392
11/28/21	8451	7488	3483	21115	18753
12/5/21	7653	6495	2766	22515	19025
12/12/21	6987	5644	2186	24170	19361
12/19/21	6422	4885	1750	26106	19803
12/26/21	5954	4277	1422	28361	20404
1/2/2022	5532	3718	1161	30645	21087

Weekly Hospitalizations

Week Ending	Adaptive	Adaptive-VaxOpt	Adaptive-SurgeControl	Adaptive-FallWinter 2020	Adaptive-FallWinter 2020-VaxOpt
10/3/21	1418	1418	1418	1441	1441
10/10/21	1276	1276	1276	1361	1361
10/17/21	1154	1153	1153	1310	1311
10/24/21	1033	1031	981	1274	1273
10/31/21	940	934	772	1282	1278
11/7/21	852	839	579	1309	1291
11/14/21	773	748	449	1353	1313
11/21/21	703	665	354	1418	1346
11/28/21	640	589	279	1501	1385
12/5/21	580	515	223	1598	1420
12/12/21	528	451	175	1713	1459
12/19/21	484	393	140	1845	1496
12/26/21	445	342	112	1994	1540
1/2/2022	410	298	90	2157	1592

Overview of relevant on-going studies

Other projects coordinated with CDC and VDH:

- **Scenario Modeling Hub:** Consortium of academic teams coordinated via MIDAS / CDC to that provides regular national projections based on timely scenarios
- **Genomic Surveillance:** Analyses of genomic sequencing data, VA surveillance data, and collaboration with VA DCLS to identify sample sizes needed to detect and track outbreaks driven by introduction of new variants etc.
- **Mobility Data driven Mobile Vaccine Clinic Site Selection:** Collaboration with VDH state and local, Stanford, and SafeGraph to leverage anonymized cell data to help identify

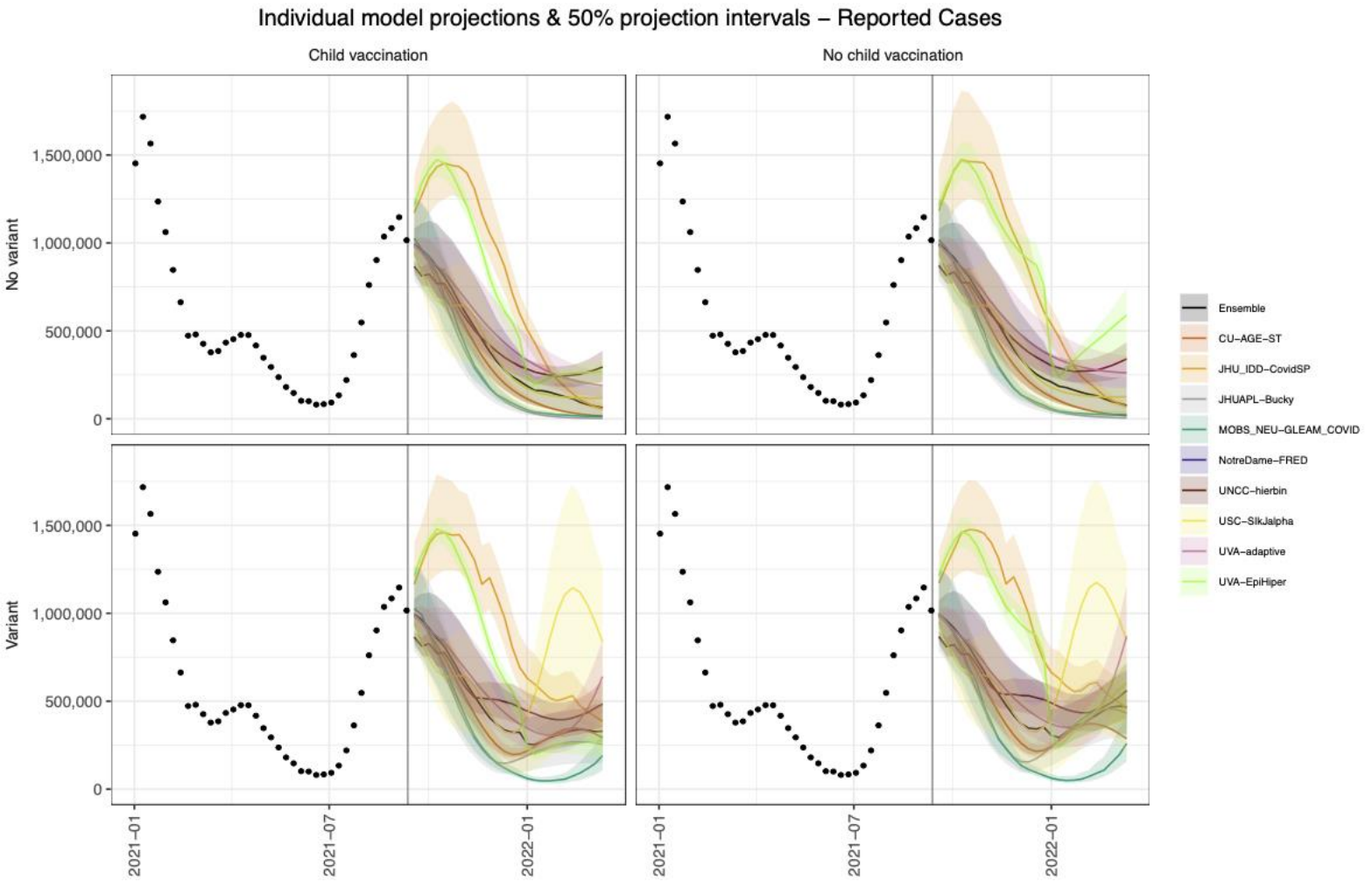
COVID-19 Scenario Modeling Hub

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios that vary vaccine rates (high – low) and impact of the Delta variant (high and low)

- Round 9 released to assist in support of 5-11 vax consideration (ACIP meeting Sept 22-23)
- Rounds 4-8 now available

Round 4 Results were published May 5th, 2021 in MMWR

https://covid19scenariomodelinghub.org/viz.html



COVID-19 Scenario Modeling Hub – Round 7

Round 7 scenarios explore the effects of a variant similar to Delta (B.1.617.2) against different backgrounds of vaccination. Includes some vax escape

Vaccinations in 5-11 start in Nov

- Follows same rates as adolescents

Emerging Variant Impact (5% prevalence on Nov 15)

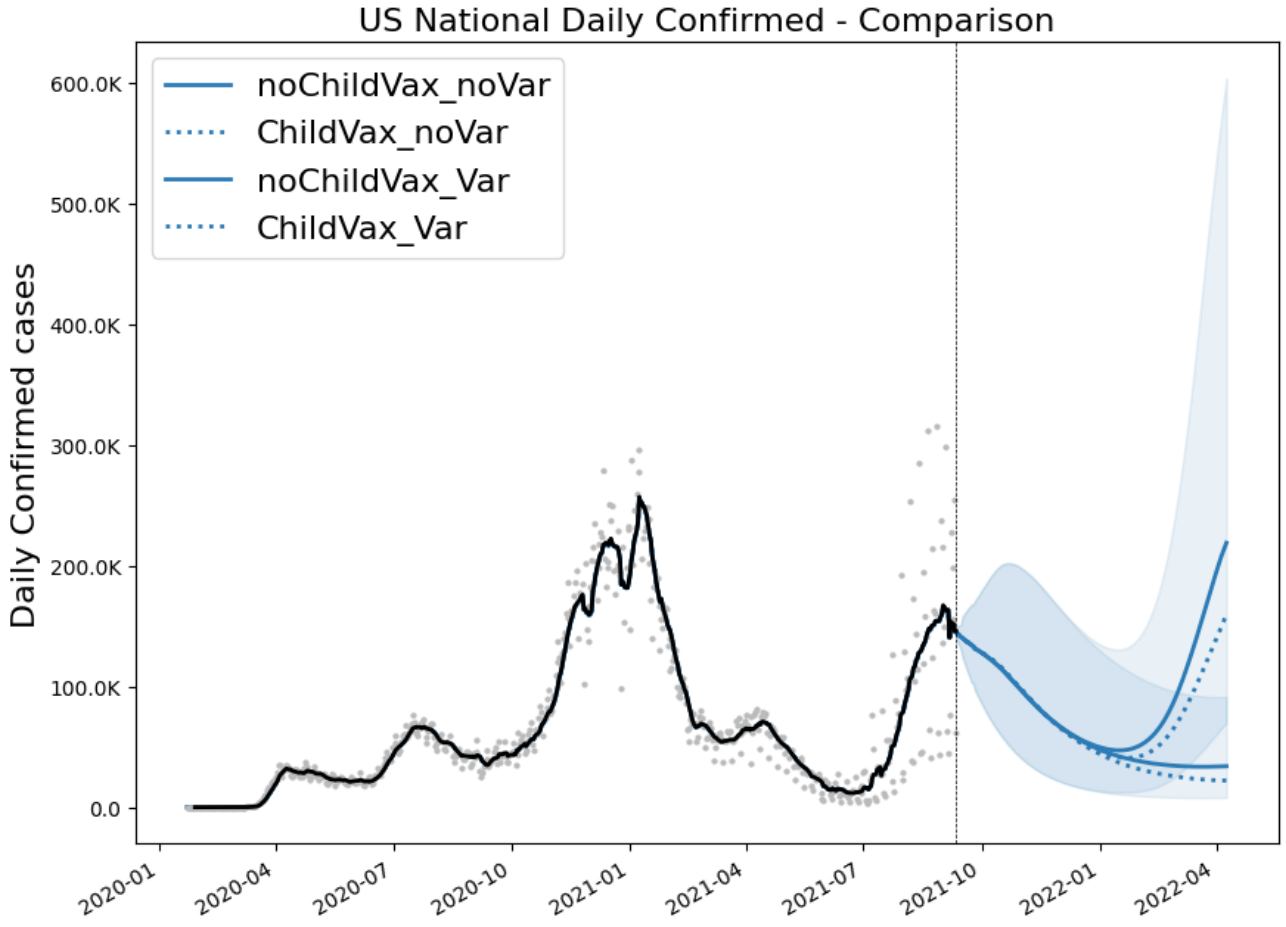
- 50% boost as it eventually predominates

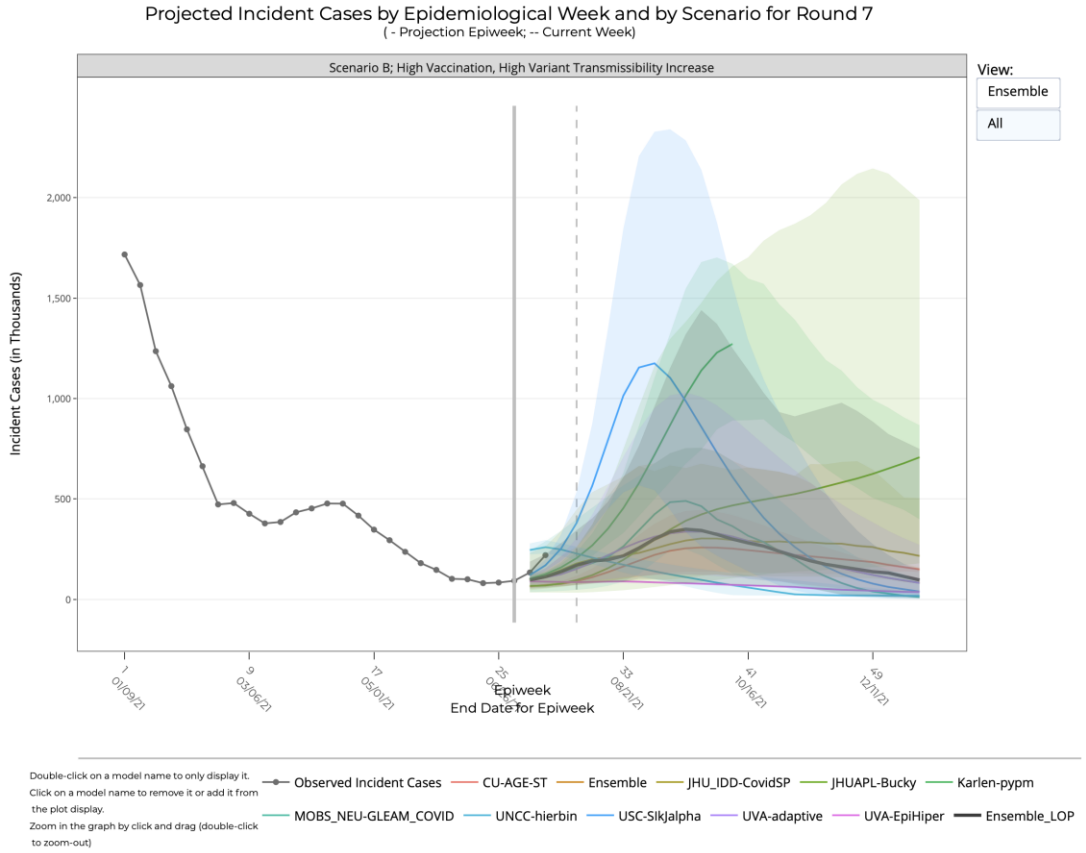
We consider a 2x2 scenario design, where childhood vaccination (5-11 years) is on the first axis, and a change in virus transmissibility is on the second axis. The second axis reflects a stress test, illustrating the potential impact of a new variant arising during the projection period:

	The same mix of variants circulate throughout the projection period. No change in virus transmissibility.	A more transmissible variant emerges, comprising 1% of circulating viruses on **Nov 15**. The new variant is **1.5X** as transmissible as viruses circulating at the beginning of the projection period.
Vaccination among 5-11yrs is approved and immunization begins on Nov 1. Each state's uptake rate reflects the percent coverage increases observed for 12-17-year-olds since distribution began on May 13.	A	C
No vaccination for children under 12	B	D

https://covid19scenariomodelinghub.org/viz.html

Modeling Hub – Round 9 Prelim Results

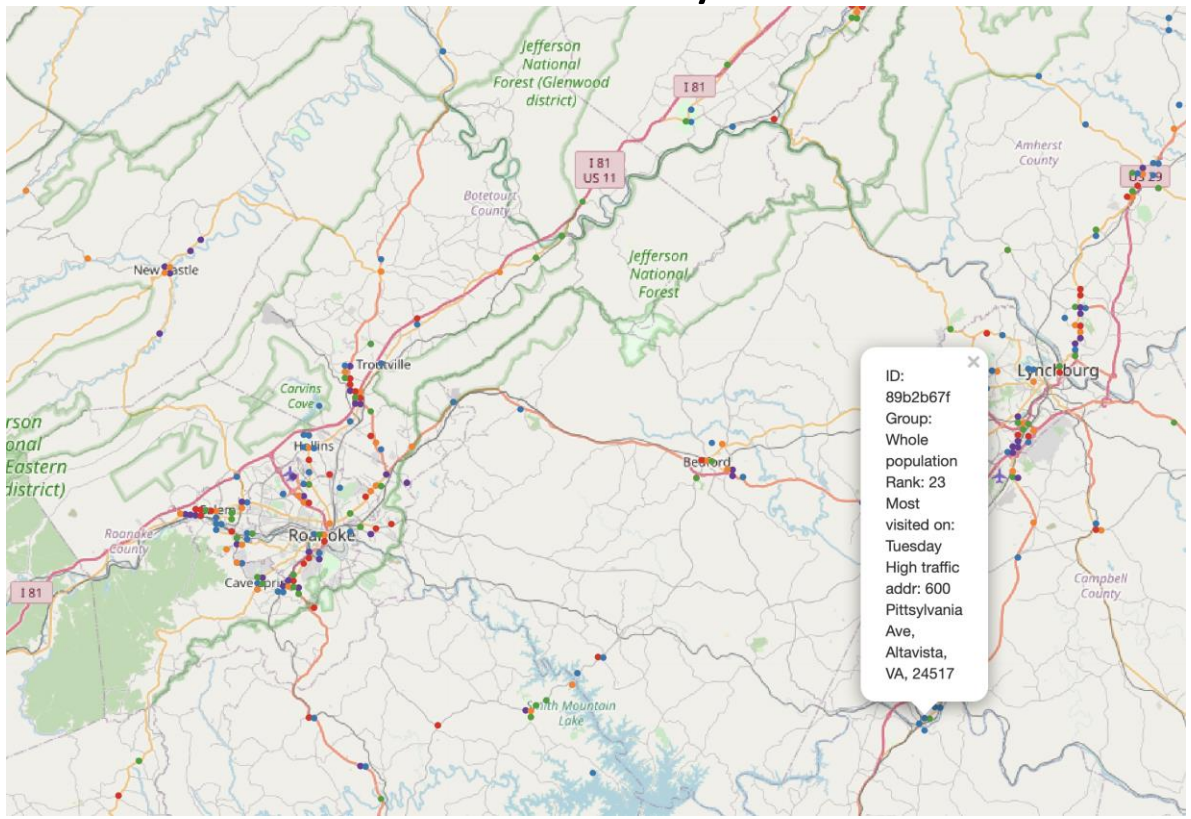




https://covid19scenariomodelinghub.org/viz.html

Data Recommended Mobile Vax Clinic Sites

Detailed and Timely Locations



Data Delivered and Disseminated to Locals

Provides a list of areas most visited by a given demographic group based on SafeGraph mobility data that links visits to specific sites and the home Census Block Group of the anonymized visitors

Demographic Groups: Black, Lantinx, Young Adults (20-40), Unvaccinated, and Whole Population

Data Included: Rank, Weight, most visited Day of Week, Highly Visited Address, and Lat-Long of area

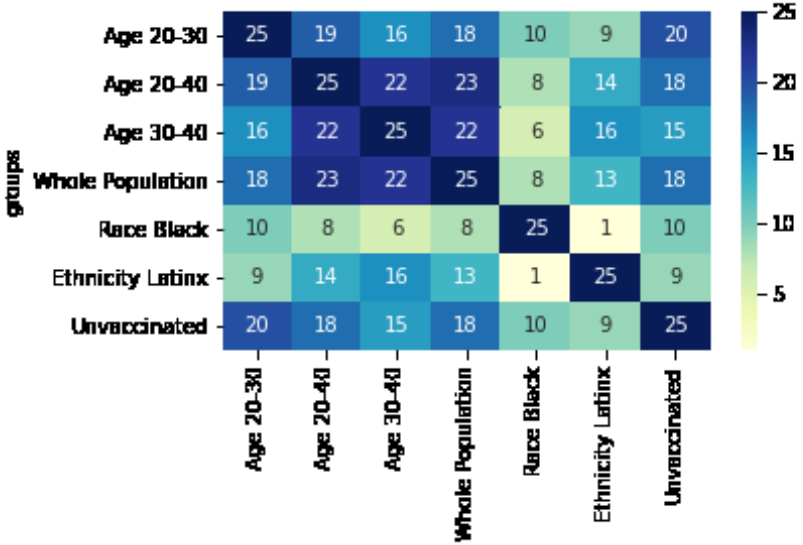
Goal: Provide frequently visited locations based on populations and vaccination levels one desires to reach

Example: List of location in the Southside frequented by 20-40 year olds

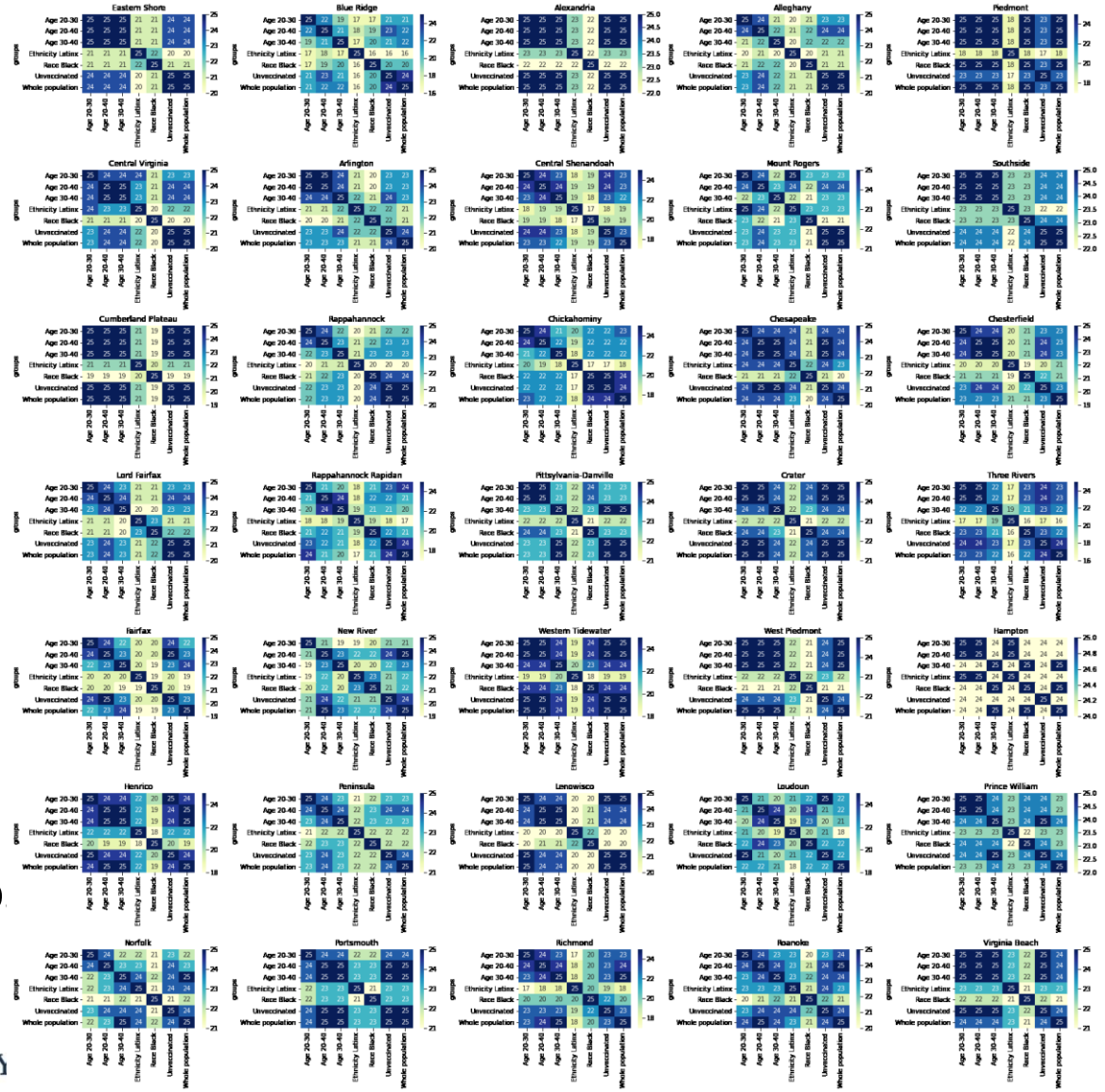
Data Recommended Mobile Vax Clinic Sites

Overlap of locations between groups

State Level



Within VDH Health Districts



Different groups visit different areas

- Least overlap between Black and Latinx
- Overlap in ages highest, but drops with large gap
- Districts have different overlap patterns

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Venkatramanan, S., et al. "Optimizing spatial allocation of seasonal influenza vaccine under temporal constraints." *PLoS Computational Biology* 15.9 (2019): e1007111.

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Biocomplexity Institute. COVID-19 Surveillance Dashboard. https://nssac.bii.virginia.edu/covid-19/dashboard/

Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/

Biocomplexity page for data and other resources related to COVID-19: https://covid19.biocomplexity.virginia.edu/

Questions?

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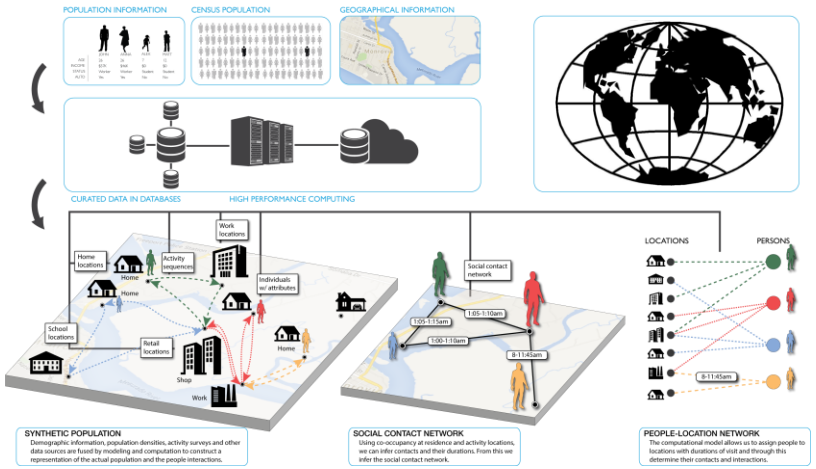
Supplemental Slides

Agent-based Model (ABM)

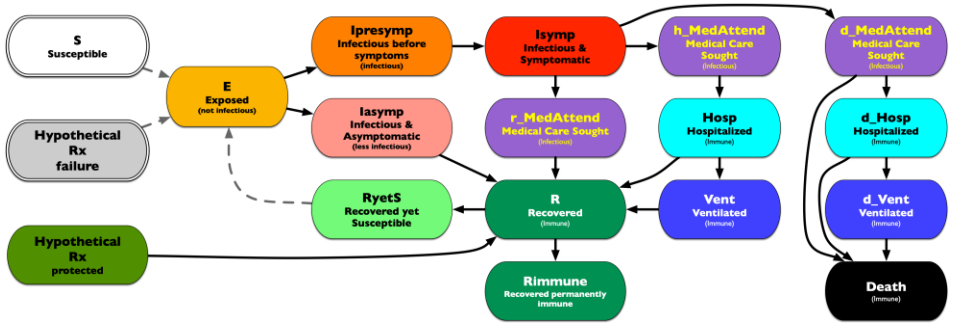
EpiHiper: Distributed network-based stochastic disease transmission simulations

- Assess the impact on transmission under different conditions
- Assess the impacts of contact tracing



Synthetic Population

- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations



Detailed Disease Course of COVID-19

- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments